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JULIUS O. SCHLOTTERBECK, PH.D.  
(1865—1917)

# A TEXT-BOOK OF INORGANIC PHARMACEUTICAL CHEMISTRY

BY

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*Fourth Edition, Thoroughly Revised  
With 23 Illustrations*



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## PREFACE TO THE FOURTH EDITION

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THIS work has been revised so that it may be used advantageously with the United States Pharmacopœia XIII and National Formulary VIII by students of pharmacy and pharmacists.

It will be noted that several important changes have been made in the content of the book. Quantitative determinations have been deleted. A reference is made to or a cursory description is given of commercial methods of manufacture that are of historical value only. Industrial processes in current use are described in more or less detail. The chemical properties and pharmacological actions of the elements and their compounds have been elaborated upon. Also, the discussions of the therapeutic value and uses of the individual compounds and their pharmaceutical preparations have been extended. Only those official salts of organic acids in which the inorganic portion of the molecule contributes the therapeutic activity have been included for discussion. For example: sodium salicylate has been deleted, whereas mercuric salicylate has been retained. In addition, however, there are a number of compounds of an inorganic-organic nature, *e. g.*, organic combinations with I, Au, Hg, As, Sb, Bi, etc., whose therapeutic activity depends upon the inorganic portion of the molecule. Such combinations have been effected in order to (1) minimize toxicity and (2) to give a retarded or delayed action to the inorganic component of the molecule. The authors believe that discussions of this type of compound do not fall within the scope of this text. For information about these compounds, reference should be made to standard textbooks in the organic field. There has also been included a number of interesting non-official inorganic compounds having some therapeutic value. In inorganic pharmaceutical chemistry courses, it is customary for the instructor to assign a number of problems. Therefore, a table of four place logarithms is appended for the convenience of the student.

A number of our contemporaries and also chemical and pharmaceutical manufacturers have been very helpful by keeping us advised of new developments in their fields. They have our sincere thanks. Especially do we want to express our appreciation and thanks to Dean Emeritus S. C. Lind for bringing the chapter on Radioactivity and The Radioactive Elements up-to-date.

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MINNEAPOLIS, MINNESOTA

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# Inorganic Pharmaceutical Chemistry

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## CHAPTER I

### OXYGEN AND OZONE

#### OXYGEN

*Oxygen*, U. S. P. XIII

Symbol, O. Valence, 2. Atomic Weight, 16; Atomic Number, 8

**History.**—Duckworth's study of an old work on chemistry by Klaproth led him to conclude that the Chinese, as early as the eighth century, recognized the existence of an active element in the air. They designated it as *yne* and believed it to be a component of water. Its action upon various metals and also its power to combine with sulfur and carbon were known to them. Furthermore, they made the substance by heating saltpeter and certain minerals, such as native manganese dioxide.

The phenomenon of combustion was studied during the fifteenth century by Leonardo da Vinci. In 1668, Mayow determined the amount of a particular gas present in the atmosphere, and showed that it was consumed during oxidation and during the respiration of animals. He concluded that these processes were analogous. In 1727, Steven Hales obtained oxygen by strongly heating minium ( $Pb_3O_4$ ), but apparently did not realize that he had obtained a new element. In 1774, Bayen obtained the gas from mercuric oxide. In August of the same year, J. Priestley published a description of the properties of a gas which he obtained by heating mercuric oxide. He called it "dephlogisticated air." K. W. Scheele, a Swedish apothecary, working independently during the years 1771 to 1773, also announced in 1777 the discovery of this element which he called "empyreal air." He prepared the gas from nitrates, observed many of its properties and contributed much to the knowledge of this element. A. L. Lavoisier, a French chemist of great renown, repeated Priestley's experiments and correctly interpreted the part played by oxygen in combustion, respiration, etc. Because of the acidic nature of many of the compounds formed by the combustion of substances in this gas, he named the element "oxygen," from the Greek:  $\delta\xi\psi\sigma$ , sour;  $\gamma\epsilon\nu\nu\alpha\omega$ , I produce.

**Occurrence.**—Oxygen in the free state constitutes 20.9 per cent by volume (nearly 23.1 per cent by weight) of the atmosphere. In combination with other elements it is found in very large quantities. About 88.81 per cent by weight of water is oxygen and nearly 50 per cent by weight of terrestrial matter is composed of it. Growing plants possess the power of absorbing carbon dioxide from the air, assimilating the carbon and liberating the oxygen. Oxygen is necessary to animal life in every form.

**Physical Properties.**—Oxygen is a colorless, tasteless and odorless gas. It is slightly heavier than air, its density being 1.10532 (air = 1). One liter of oxygen weighs 1.429 Gm. at 0° C. and 760 mm. pressure. Oxygen can be liquefied when cooled below -118.82° C., which is its critical temperature. The *critical temperature* of a gas is that temperature at or below which it can be liquefied by pressure, but above which it cannot be liquefied regardless of the pressure applied. The *critical pressure* of a gas is that pressure which will just liquefy a gas at its critical temperature. Liquid oxygen has a density of 1.13, boils at -182.96° C., and may be frozen to a light blue solid which melts at -218.4° C. One volume of oxygen dissolves in approximately 32 volumes of water and in about 7 volumes of alcohol, at 20° C. and at 760 mm. pressure. It quite readily dissolves also in some molten metals, especially silver.

**Chemical Properties.**—Oxygen is one of the most active elements. It unites directly with most metals and non-metals, the rapidity of the reactions depending upon the purity and temperature of the gas. The presence of a catalyst<sup>1</sup> greatly stimulates the combination. Non-metals, *e. g.*, sulfur, phosphorus, and carbon, combine with oxygen to form oxides (1, 2 and 3).

- (1)  $S + O_2 \rightarrow SO_2$
- (2)  $4P + 5O_2 \rightarrow 2P_2O_5$
- (3)  $C + O_2 \rightarrow CO_2$

At high temperatures, oxygen unites with several other non-metals (silicon, boron and arsenic). Union between oxygen and nitrogen takes place only at exceedingly high temperatures (1900° C.) and then only to a limited degree (1 per cent or less). Oxygen does not combine *directly* with the halogens or the inert gases (He, Ne, A, Kr, Xe, Rn), although the oxides of chlorine and iodine can be prepared by other chemical methods. All of the common metals, excepting gold, silver, and platinum, when heated, combine with oxygen with varying degrees of avidity.

**Official Tests for Identity.**—1. A glowing splinter of wood bursts into flame when it is introduced into oxygen.

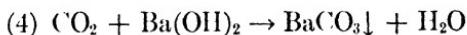
<sup>1</sup> A catalytic agent is "a substance which accelerates whether positively or negatively, the speed of a chemical reaction by contact or by entering into the reaction, the agent having the same chemical composition at the end of the change as at the beginning." (General Inorganic Chemistry, by Sneed and Maynard, p. 75.)

2. If a small coil of iron picture wire is heated to redness and then inserted into a vessel containing oxygen, it will burn with great brilliance.

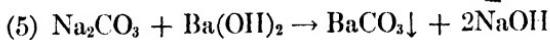
**Tests for Purity.**—The U. S. Pharmacopœia XIII recognizes oxygen under the title Oxygen (Oxygenium), requires that it contain 99 per cent by volume of O<sub>2</sub>, and limits the presence of carbon dioxide, halogens, acids or alkalies, and oxidizing substances. NOTE.—Cylinders containing oxygen must be kept at a temperature of 25° C. ± 2° for at least six hours before the Oxygen is withdrawn for the following determinations. Gas volumes for the following tests and assays are to be corrected to a pressure of 760 mm. and a temperature of 25° C.

*Acids or Alkalies.*—Dilute 0.3 cc. of methyl red T.S. with 400 cc. of boiling water, and boil the solution for five minutes. Pour 100 cc. of the boiling solution into each of three color-comparator tubes of clear glass, of approximately the same size and marked "A," "B," and "C," respectively. Add 0.2 cc. of 0.01 N hydrochloric acid to tube "B," and 0.4 cc. of 0.01 N hydrochloric acid to tube "C." Stopper each of the tubes, and cool them to room temperature. Pass 2000 cc. of Oxygen through the solution in tube "B" at a rate requiring about thirty minutes for the passage of the gas. The color of the solution in tube "B" is no deeper red than that of the solution in tube "C" and no deeper yellow than that of the solution in tube "A". Comparisons are best made using a colorimeter. Tube "B" contains 0.0000729 Gm. of hydrogen chloride, if the alkali impurity were ammonia gas the maximum allowable would be 0.000034 Gm. of ammonia in the 2000 cc. of Oxygen sample. In the same way the gaseous acid component could not be more than 0.0000729 Gm. of gaseous hydrogen chloride or 0.000128 Gm. of gaseous sulfur dioxide.

*Carbon Dioxide.*—Pass 1000 cc. of Oxygen through 50 cc. of barium hydroxide T.S. The test solution must be devoid of turbidity prior to the test. If carbon dioxide is present a white precipitate forms (4).

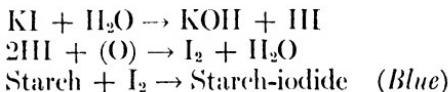


Regulate the flow so as to require fifteen minutes for the delivery of 1000 cc. of gas. The delivery tube must have an orifice approximately 1 mm. in diameter and must extend to within 2 mm. of the bottom of the vessel containing the barium hydroxide solution. The vessel employed must give a hydrostatic column of from 12 to 14 cm. with the 50 cc. of the solution. The turbidity produced, if any, does not exceed that produced when 1 cc. of a solution prepared by dissolving 0.1 Gm. of sodium bicarbonate in 100 cc. of freshly boiled and cooled distilled water, is added to another 50 cc. portion of barium hydroxide T.S. under like prescribed conditions (5).

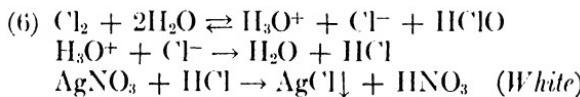


For a more precise control use the turbidimetric technique, U. S. P. XIII, page 709.

*Oxidizing Substances.*—Pass 2000 cc. of Oxygen, under conditions comparable to those in the test for *carbon dioxide*, through 15 cc. of freshly prepared starch-potassium iodide T.S. to which has been added 1 drop of glacial acetic acid. The color of the test solution is not altered by the passage of the Oxygen, as shown by comparing it with another portion of the acidified starch-potassium iodide T.S. through which the gas has not been passed. Oxidizing substances present as impurities may be detected by the blue color which they produce in an acidified starch-iodide T.S. The possible reaction may be represented as follows:



*Halogens.*—Pass 2000 cc. of Oxygen under conditions comparable to those in the test for *carbon dioxide*, through a mixture of 100 cc. of distilled water and 1 cc. of silver nitrate T.S. The liquid shows no greater degree of opalescence than does a mixture of 100 cc. of distilled water and 1 cc. of silver nitrate T.S., prepared at the same time as that through which the gas passes, the observation being made in 100 cc., low-form Nessler tubes, which are closely similar in all respects. A positive test using chlorine as the halogen is (6).



*Carbon Monoxide.*—Oxygen meets the requirements of the test for *Carbon Monoxide in Oxygen*, page 626 of U. S. P. XIII. Nitrogen which is negative to the test for *Carbon Monoxide* under *Ethylene*, page 213 of U. S. P. XIII, shall be considered as carbon monoxide-free for the purpose of this test. The test depends upon the reaction between sodium hydrosulfite and oxygen in a closed system (7)



which results in leaving any carbon monoxide present mixed with nitrogen which is introduced during the assay. Upon the addition of diluted blood to the mixture of gases, a pink or bright red color develops if carbon monoxide is present.

Pyrogallic acid-tannic acid mixture causes a dirty olive-green precipitate with the oxyhemoglobin when carbon monoxide hemoglobin is absent.

*Commercial Manufacture.*—Oxygen is now or has been manufactured on a large scale for commercial purposes by the following processes: (1) By the fractionation of liquid air; (2) the electrolysis

of water; (3) the Boussingault-Brin Brothers' process; (4) the Thessie du Motay-Marechal process.

1. *The Fractionation of Liquid Air—Linde Process.*—This process is based upon the fractional distillation of liquefied air and has superseded all other processes for the commercial production of oxygen. When air is liquefied in a suitable apparatus, it boils at a temperature of about  $-191^{\circ}$  C. The boiling-point of liquid air ( $-191^{\circ}$  C.) is higher than the boiling-point of liquid nitrogen ( $-195.8^{\circ}$  C.) and lower than the boiling-point of liquid oxygen ( $-182.96^{\circ}$  C.), hence the nitrogen evaporates from liquid air much more rapidly than does the oxygen. The "boiling off" of the nitrogen from liquid air may be so thoroughly accomplished that a liquid oxygen of better than 96 per cent purity may be obtained.

The commercial production of oxygen from air involves two general procedures, *viz.*: (a) *The purification and compression of air*, and (b) *the liquefaction and fractionation of the product*.

(a) Before going to the compressors, all dust and carbon dioxide must be removed from the air. Atmospheric moisture is removed at some several stages during the compression. The dust and carbon dioxide are taken out by passing the air upward through two towers working in series. These towers are packed with coke over which trickles a solution of caustic soda or potash. After its downward passage over the coke, the caustic liquor is returned to the top of the towers and used over again. Over 99 per cent of the moisture in the air is removed by liquefaction as the air is cooled in its passage from one compression cylinder to another. The small amount of water still remaining in the so-called "fourth-stage air" is removed in a cylindrical vessel, using the counter-flow principle, with fused calcium chloride or caustic potash. The compressing of the purified air is accomplished in either four- or five-stage compressors (depending on the output of the plant). In its passage from one cylinder to the next in the compressor, the air passes through a set of coils immersed in running cold water so that it enters the next cylinder at practically room temperature. In the compressor the air is reduced to about 2 per cent of its volume and is under a pressure of about 2900 pounds per square inch (about 200 atmospheres).

(b) The clean, dry carbon dioxide-free, high-pressure air is now ready to be liquefied and fractionated. These operations are usually effected in a combination liquefier and fractionator. Due to the consumption of heat necessary to overcome molecular cohesion, all gases upon expansion become somewhat cooled. The lower the temperature of a gas, the greater is the attraction between the molecules. Because more heat is required to overcome this increased cohesion, the cooling effect upon expansion is greater. The various processes for the liquefaction of air are based upon this principle. Referring to Figure 1, the high-pressure air enters the Linde system double column liquefier and separator at 1, and passes through the exchanger through coil 2. In the exchanger

the incoming air loses heat to the outgoing oxygen and nitrogen contained in their respective tubes, so that when it reaches the expansion valve at 3, it liquefies and flows down over the plates in the lower column. A liquid rich in oxygen collects at 4 and a

liquid high in nitrogen reaches the top of the lower column, is cooled, and collects at 7; from where it passes through the valve 8 and to the top of the upper column. The liquid rich in oxygen, on the other hand, passes through the valve and tube 10 to the middle of the upper fractionating column. As this liquid passes down through the upper column it loses its nitrogen and collects at 5. The nitrogen being the more volatile of the two liquids leaves at the top of the upper column. Both of the gases leave the system through the exchanger *via* their respective conduits, 6 and 9. The oxygen is delivered either to a large tank or directly to a three-stage compressor which compresses the gas in seamless steel cylinders under a pressure of 2000 pounds to the square inch. Liquid oxygen is now being delivered as such to large users of the gas.

2. *The Electrolysis of Water.*—In those plants where both oxygen and hydrogen are needed, this method may be used successfully. A direct current is passed between iron or steel electrodes that are

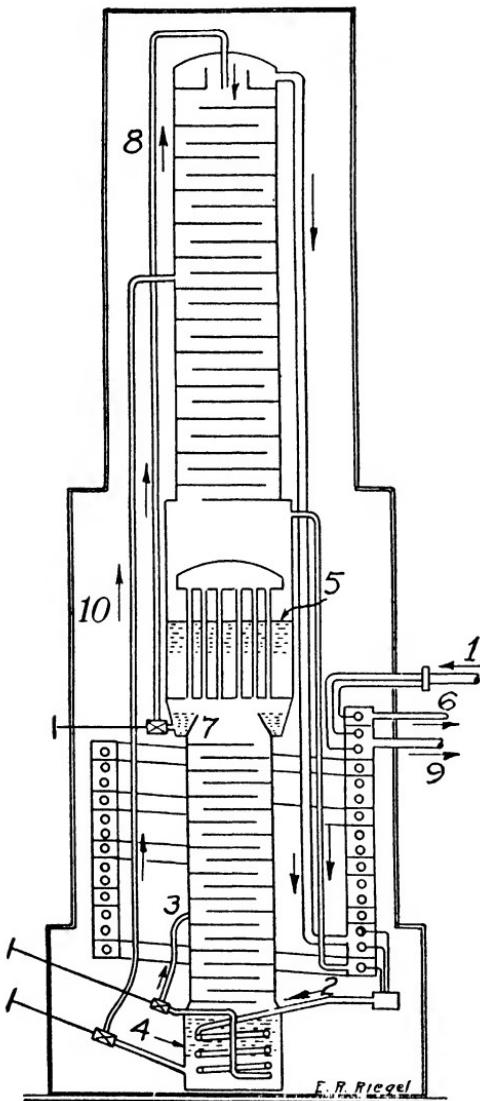
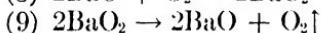
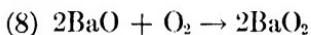


FIG. 1. — Combined liquefier and separator.  
(From Riegel's Industrial Chemistry—An Introduction, Publ. Chemical Catalog Co., Inc.)

immersed in 15 per cent aqueous solution of sodium or potassium hydroxide, using an asbestos cloth diaphragm. Oxygen is generated at the anode and hydrogen at the cathode; the method of collecting

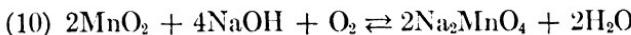
the gases depending upon the construction of the cell. Water only must be added to the cell during the electrolysis. The efficiency of this type of cell (said to yield an average of about 7.5 cubic feet of hydrogen and 3.8 cubic feet of oxygen per kilowatt hour) is increased by carrying out the electrolysis under pressure.

*3. The Boussingault-Brin Brothers' Process.*—Although practically obsolete, the Boussingault process, as modified by the Brin brothers, is of historical interest. It was carried out by heating barium oxide to dull redness in retorts into which clean dry air, free from carbon dioxide, was forced under a pressure of about 15 pounds to the square inch. Under these conditions, 1 molecule of barium oxide combined with 1 atom of oxygen to form barium peroxide (8). When the reaction was complete, the pressure was released and most of the uncombined nitrogen escaped. While the temperature of the barium peroxide was still very high, a vacuum of about 27 inches was produced in the retort by a suitable pump. Under these conditions, 2 molecules of the peroxide yielded 1 molecule of oxygen and were reconverted to the oxide (9). The process was a continuous one, the barium oxide being changed about once every 6 months.



*4. The Thessie du Motay-Marechal Process.*—This process is also of historical interest rather than of industrial importance.

It consisted of making sodium manganate by passing dry air over a heated mixture of manganese dioxide and sodium hydroxide (10). When the mass was mixed with a little cuprous oxide to insure regularity in the reaction and heated to 450° C. in a current of steam, manganese dioxide and sodium hydroxide were regenerated and oxygen was liberated.



The oxygen was washed with a cold alkaline solution and collected in gasometers, from which it was subsequently compressed in steel cylinders at about 1800 pounds pressure.

**Physiological Properties and Medicinal Uses.**—Oxygen is essential to all animal life. During respiration it combines with the hemoglobin of the blood to form oxyhemoglobin, in which form it is distributed to the tissues of the body, where compounds containing carbon and hydrogen are slowly oxidized to carbon dioxide and water, and heat (energy) is developed. Oxygen is widely used in medical practice as well as in surgery. All pathological conditions, *e. g.*, pneumonia, angina, asthma, bronchitis, etc., that are accompanied by cyanosis and dyspnea (difficulty in breathing) are relieved by inhalations of the gas, using the "oxygen tent" or other suitable devices. It is administered in chloroform poisoning and in threatened death from inhalations of coal gas or nitrous oxide (*q. v.*). Oxygen is used in the resuscitation of individuals apparently

drowned. Under conditions in which there is a scarcity of oxygen, *e. g.*, in airplanes at high altitudes, in diving bells and in submarines, this essential gas is supplied from tanks.

Oxygen is of great importance in industry because of its use in oxyacetylene torches for steel welding and steel cutting. Liquid oxygen mixed with powdered charcoal has to some extent been used as an explosive but as such has not been very widely used. Recently liquid oxygen has been most useful as an ingredient in the fuel of rockets.

### OZONE

Formula,  $O_3$ . Molecular Weight, 48

**History.**—In 1785, Van Marum, a Dutch chemist, called attention to the fact that oxygen or air, through which electric sparks had been passed, possessed a peculiar, irritating odor and also the property of tarnishing mercury. In 1840, the German chemist, Schönbein, demonstrated that these phenomena were caused by a new gaseous substance formed from oxygen during the electrical discharge, and he named it *ozone* from the Greek, *to smell*. He prepared fairly high concentrations of the gas in oxygen by the electrolysis of water and also by the slow combustion of phosphorus. In 1856, Andrews established the constitution of ozone.

**Occurrence.**—Ozone is found in very small quantities in the atmosphere. Electrical discharges through the air (lightning) produce ozone. The characteristic odor of the gas is usually very pronounced around electrical generating machines in operation.

**Physical Properties.**—Ozone is a bluish gas having a peculiar, irritating odor (suggesting sulfur dioxide). One liter of ozone weighs 2.144 Gm. at  $0^\circ C.$  and 760 mm., and is, therefore, one and a half times heavier than oxygen (1.429 Gm. to the liter). When a mixture of ozone and oxygen is cooled with liquid oxygen, the ozone condenses to a blue liquid, which boils at  $-112^\circ C.$  and freezes at  $-251^\circ C.$  Both liquid ozone and liquid oxygen are strongly magnetic. Ozone dissolves in and unites with oil of turpentine, oil of cinnamon and olive oil to form ozonides, some of which possess antiseptic properties.<sup>1</sup>

**Chemical Properties.**—The transformation of oxygen into ozone involves the changing of electrical energy into chemical energy. The energy, expressed as heat units, required to change 3 molecules (96) of oxygen into 2 molecules (96) of ozone is 68,820 calories (1).

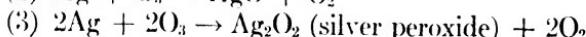


Oxygen	Ozone
(96)	(96)
(3 volumes)	(2 volumes)

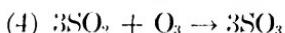
From this thermo-chemical equation it is evident that a definite weight of ozone contains more internal energy than does an equal

<sup>1</sup> J. A. Ph. A. Sci. Ed., 36, 278 (1947).

weight of oxygen, and it may be correctly concluded that ozone is a more active chemical agent than is oxygen. Unlike oxygen, ozone at ordinary temperatures oxidizes certain metals, *e. g.*, mercury (2) and silver (3).



From equations (2) and (3) it may appear that one-third of the "oxygen" of ozone is more active than the remaining two-thirds. However, the fact that 1 molecule of ozone completely oxidizes 3 molecules of sulfur dioxide to sulfur trioxide (4) indicates that *all* of the "oxygen" of ozone is chemically active and not merely one-third, as might be concluded from the above equations.



Ozone is fairly stable at very low temperatures. At ordinary temperatures it slowly decomposes into oxygen. The velocity of this chemical change increases as the temperature increases until, at about 250° C., the decomposition is complete. Van't Hoff's law of mobile equilibrium states that when the temperature of a system in equilibrium is raised, the equilibrium is displaced in the direction that absorbs heat. From this law it follows according to the thermo-chemical equation (1) that more ozone is formed the higher oxygen is heated. The presence of a catalyst causes ozone to decompose violently.

**Tests for Identity.**—1. Ozone in the atmosphere may be identified by its characteristic odor.

2. When a piece of absorbent paper that has been moistened with starch test solution containing a little sodium or potassium iodide is introduced into an atmosphere containing ozone, the starch is colored blue due to liberated iodine (5).



Oxides of nitrogen, the halogens, and particularly acidulated hydrogen peroxide liberate iodine from iodides and are, therefore, interfering substances.

3. A piece of red litmus paper, one-half of which has been dipped into a solution of potassium iodide, will turn blue when held in an atmosphere containing ozone. This is caused by the hydroxide formed by the action of ozone upon potassium iodide (5).

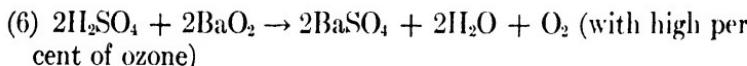
4. Slightly heated silver is tarnished by ozone.

**Preparation of Ozone.**—1. Ozone is prepared by subjecting cold, dry oxygen or air to an electric discharge. The apparatus used for this purpose is called an *ozonizer*, and consists of 2 glass tubes, one within the other.<sup>1</sup> The outside of the outer tube is covered with tin-foil and the inner tube is lined with the same material. The

<sup>1</sup> See Tindal Ozonizer in Thompson's Theoretical and Applied Electrochemistry, p. 515.

electrical discharge is produced through the space between the tubes by connecting the foils with the poles of an induction coil. Cold, dry, carbon dioxide-free oxygen or air is slowly passed between the tubes where, under ordinary conditions, from 5 to 6 per cent of the oxygen is converted into ozone. Under the most favorable conditions, *e. g.*, using a silent discharge, low temperature and very pure, dry oxygen, the yield of ozone can be increased to better than 18 per cent.

2. Ozone is formed in small quantities by: (a) Slow oxidation (especially of phosphorus and zinc); (b) by the electrolysis of dilute sulfuric acid; (c) by the action of an active acid, *e. g.*, sulfuric acid upon a highly oxidized compound, *e. g.*, barium peroxide (6); (d) by burning hydrogen in oxygen; (e) by plunging a heated platinum coil into liquid oxygen; and (f) by the decomposition of potassium chlorate.



**Uses.**—The more improved industrial methods for preparing this active oxidizing agent have made possible its utilization in the arts and industries. Ozone *per se* is rarely used, but air or oxygen containing it is employed as a bleaching agent for oils, waxes, delicate silk or wool fabrics, flour, starch, ivory, etc.; as a disinfectant for drinking water; and as a deodorant of foul animal matter, especially in ventilating large public halls and food warehouses. It is also used in the manufacture of synthetic camphor and many other organic compounds. It is said that 13 parts of ozone per 1,000,000 is necessary for an antiseptic action.<sup>1</sup> One part of ozone per 1,000,000 is tolerated by man. Ten parts per 1,000,000 when inhaled for fifteen minutes produces headache and sore throat, and exposure to this concentration for several hours is dangerous to life. Unlike carbon monoxide, ample warning is given by headache, cough and general pulmonary irritation.

<sup>1</sup> Proc. Roy. Soc., **84**, 404, 573 (1911).

## CHAPTER II

### HYDROGEN

Symbol, H. Valence, 1. Atomic Weight, 1.008; Atomic Number, 1

**History.**—There is evidence that hydrogen was recognized by Paracelsus in the sixteenth century. During the seventeenth century, Turquet de Mayenne called attention to its combustible nature, and in 1700 N. Lemery showed that upon ignition a mixture of hydrogen and air detonated. The first experiments to determine the nature of hydrogen were made by Cavendish in 1766. He produced it by the action of dilute hydrochloric or sulfuric acids upon certain metals, and called the gas “inflammable air,” which name conformed to the generally accepted “phlogiston” theory of the day. (See p. 83.) Later (1781), Cavendish and Watt showed that water was the only substance produced when hydrogen was burned in air or oxygen and, as oxygen was then known to be the substance with which combustibles united, they correctly concluded that water was a compound of hydrogen and oxygen. In 1783, Lavoisier named the gas *hydrogen*, from the Greek, *ὕδωρ*, water, and *γεννάειν*, to produce.

**Occurrence.**—Very small quantities of hydrogen are found in the free state in some volcanic gases, in fumaroles and in pockets in carnallite and rock salt deposits. It also occurs in very small quantities in the air, in some meteorites, in the stars and nebulae and in the envelopes of the sun. Hydrogen is sometimes a product of the decomposition of organic matter. It is produced also by anaërobic fermentation. Hydrogen is an integral part of many compounds, minerals, and most animal and vegetable tissues. It is an essential constituent of all acids.

**Physical Properties.**—Pure hydrogen is a colorless, tasteless and odorless gas. It has a specific gravity of 0.06947 (air = 1) and is, therefore, about fourteen and a half times lighter than air. One liter of hydrogen weighs 0.08987 Gm., whereas the same volume of air weighs 1.293 Gm. At its critical temperature of  $-239.9^{\circ}$  C. hydrogen may be liquefied by a pressure of 12.8 atmospheres. Liquid hydrogen is colorless and has a boiling-point of  $-252.7^{\circ}$  C. Hydrogen has been solidified to a colorless solid melting at  $-259.14^{\circ}$  C. The specific heat of hydrogen gas is 3.4041 (water = 1). Hydrogen is only sparingly soluble in water (1.8 cc. dissolves in 100 cc. of water at  $15^{\circ}$  C.). It diffuses very rapidly through porous membranes and through some metals at red heat. Hydrogen is absorbed or “occluded” by many metals. The quantity of gas “taken up” depends upon the metal, its physical condition, and upon the temperature and pressure during the operation. At ordinary tem-

peratures and pressures, 1 volume of palladium black absorbs 873 volumes of hydrogen, whereas finely divided iron, gold, and platinum occlude 19.2, 46.3 and 49.3 volumes of the gas, respectively.

**Chemical Properties.**—At ordinary temperatures hydrogen is chemically inactive. Its activity may be greatly increased by passing it through an ozonizer (*q. v.*), by subjecting it to high potential electrical discharges in vacuum, or by exposing it to the action of alpha-rays from radium emanations. At high temperatures or in one of its activated forms hydrogen is a powerful reducing agent. When molecular hydrogen ( $H_2$ ) is passed through an electric arc it forms atomic hydrogen ( $H$ ) which again recombines to form molecular hydrogen ( $H_2$ ), liberating much heat. This knowledge is made use of in atomic hydrogen welding torches which develop temperatures of  $4000^\circ$  to  $5000^\circ$  C.

Hydrogen burns in air with a pale blue, non-luminous flame. When mixed with oxygen in a suitable burner (oxyhydrogen torch) and ignited, it burns with a flame giving very little light but a temperature of over  $2500^\circ$  C. The oxyhydrogen flame will melt all metals, even platinum. When this flame is directed upon a piece of quicklime (CaO), the latter becomes white-hot at the point of contact. The emitted light is called a "calcium" or "lime light."

Hydrogen and oxygen unite very slowly at ordinary temperatures. However, if finely divided platinum is held in the mixture, the union is hastened and the heat of the reaction is sufficient to make the platinum glow, thereby causing the explosion of the mass. Automatic lighters for illuminating gas operate on this principle.

Occluded hydrogen or hydrogen in its activated state is a vigorous reducing agent. The gas occluded by palladium (1 volume of palladium absorbs up to 873 volumes of hydrogen) is especially active in this respect and readily reduces ferric salts to ferrous salts, chlorates to chlorides, nitrates to nitrites and ammonia, etc. One of the most important uses of hydrogen with palladium (nickel, or platinum) is for the reduction of organic compounds. Hydrogen unites with many metals and non-metals to form innumerable compounds, *e. g.*,  $H_2S$ ,  $NH_3$ ,  $PH_3$ ,  $CH_4$ ,  $HCl$ ,  $CaH_2$ ,  $NaH$ , etc.

**Commercial Manufacture.**<sup>1</sup>—Hydrogen has become of increasing industrial and military value, and its manufacture has likewise assumed importance. Because it is not economical to ship unliquefied gases for long distances, the manufacture of hydrogen (a difficultly compressible gas) is, of necessity, a more or less local undertaking. Thus, the method of manufacture depends on the required purity, raw materials, power supply, etc., of the area being supplied by the hydrogen plant.

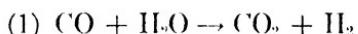
Hydrogen may be obtained by (1) the fractionation of water gas or coke oven gas; (2) catalytically oxidizing CO of water gas with steam; (3) passing steam over incandescent iron; (4) the "Silicor" process from ferrosilicon and caustic soda; (5) electrolysis of water

<sup>1</sup> Bulk Production of Hydrogen, Ind. and Eng. Chem., **30**, 1139 (1938).

containing caustic soda; (6) pyrolysis or breaking down of hydrocarbons at relatively high temperatures; (7) fermentation of corn mash in the production of acetone and butanol; (8) the reaction of water on some metals; (9) the action of caustic on some metals; (10) the decomposition of some metallic hydrides with water; and (11) catalytically breaking down ammonia. (12) It is also a by-product of the electrolytic caustic cell.

1. Water gas (a mixture of approximately equal parts of CO and H<sub>2</sub>) is cooled and compressed by the Linde method to the point where the CO liquefies and can be removed as a liquid. The same is true of coke oven gas which is a mixture composed largely of hydrogen together with other gases (mainly CH<sub>4</sub>, N<sub>2</sub>, CO, C<sub>2</sub>H<sub>4</sub>, and CO<sub>2</sub>).

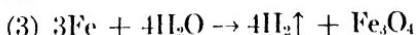
2. The carbon monoxide in water gas is removed by catalytically oxidizing it with steam to carbon dioxide, which is then dissolved out completely under pressure in cold water followed by a scrubbing with caustic soda. During the oxidation additional hydrogen is produced (1).



3. It is claimed that by the Messerschmidt process hydrogen of better than 99 per cent purity may be obtained. The process is of particular importance in the preparation of hydrogen for the hydrogenation of oils, where it is said that as little as 0.25 per cent CO in the hydrogen retards the hydrogenation. The process is based upon the decomposition of superheated steam by metallic iron with the subsequent reduction of the iron oxides so formed by a mixture of carbon monoxide and hydrogen (blue water gas). A diagrammatic representation of the Messerschmidt hydrogen generator may be found on page 608 of Rogers' *Industrial Chemistry*, Fourth Edition. Iron oxide is charged into the cylindrical iron retort and heated to a temperature of between 700° and 800° C. by burning water gas in the presence of air introduced into the checkered, brick filling. At this temperature, iron oxide reacts with the carbon monoxide and hydrogen of the water gas to form metallic iron, carbon dioxide and water (2).



When this reaction is complete the water gas and air are shut off and steam is introduced. The steam is superheated in its passage through the outer jacket, and as it ascends through the heated iron, it is reduced, producing magnetic iron oxide and generating hydrogen (3).



The hydrogen passes out of the apparatus and is cooled and freed from dust by washing with a spray of water. Carbon dioxide is removed with lime and any hydrogen sulfide present is taken out with oxide of iron.

4. In the so-called "Silicoll" process, powdered ferrosilicon (FeSi), made by the reduction of iron ores high in silicon, is added to a 20 per cent solution of caustic soda kept at a temperature between 80° and 90° C. In order to reduce the possibility of an explosion in the generator, the powdered ferrosilicon is sometimes made into a paste with water, which decomposes the phosphides present, and then is allowed to drop into the caustic liquor. This method is a rapid one for making a very pure hydrogen. It is one of the methods in use by the U. S. Army and Navy.

The reaction involved in the generation of H<sub>2</sub> is that of caustic soda on silicon or an iron alloy of silicon (4).



5. When electric power is available at low rates, and particularly when oxygen as well as hydrogen can be marketed, the electrolysis of water is the preferred process for preparing hydrogen. A very pure hydrogen is obtained by passing a direct current between iron electrodes immersed in a 10 to 25 per cent caustic soda solution. Hydrogen by this process is used mostly for making synthetic ammonia.

6. Carbon and hydrogen are the ultimate products obtained by the pyrolysis of all hydrocarbons. The various processes differ materially from one another and are dependent principally upon the type of carbon (carbon black, lampblack, etc.) desired. In general, methane or natural gas is heated either with or without a catalyst at relatively high temperatures. When either of these gases is passed through an alundum tube heated to 1300° to 1700° C., hydrogen and carbon, uncontaminated with intermediate products, are produced. In some of the other processes, iron, cobalt, and nickel (if kept clean of accumulated carbon) are employed to catalyze the production of carbon and hydrogen.

7. The production of acetone and butanol by fermenting a mash of ground, low-grade corn with the microorganism, *Clostridium acetobutylicum*, yields large quantities of a very pure mixture of hydrogen and carbon dioxide. The separation of the carbon dioxide from the hydrogen is effected almost completely by passing the gas mixture under pressure through a tower down which water trickles. The remaining traces of CO<sub>2</sub> may be completely removed with caustic soda. By burning part of this hydrogen in air, nitrogen is produced and is used, together with the hydrogen, to synthesize ammonia. If the mixed gases are passed over heated charcoal, a carbon monoxide-hydrogen mixture is obtained. This may be utilized to catalytically synthesize methanol. The energy required to separate the carbon dioxide from the hydrogen may be partly recovered by passing the solution of carbon dioxide through a Pelton wheel.

8. Certain metals, notably potassium and sodium, react very energetically with water to form the respective alkali hydroxides and hydrogen. Although sodium is the least active of the two, it

generates sufficient heat on contact with water to ignite the escaping hydrogen and cause an explosion. However, when sodium is amalgamated with mercury, or alloyed with other metals, its activity is reduced to a usable rate. An alloy, hydrone, composed of sodium and lead, is available commercially, and furnishes a convenient but expensive source of pure hydrogen.

Sodium amalgams are used as reducing agents in organic chemistry.

9. Some metals, *e. g.*, Zn, Al, Li, are acted upon by caustic and produce hydrogen (5).



10. Because of the low dry-weight of LiH and the high proportion of hydrogen, this compound is used to produce hydrogen for war use. Only heat or water is necessary to decompose the hydride. Of the other hydrides, CaH<sub>2</sub> (hydrolyte) is of use in furnishing a quick, pure source of hydrogen according to the following equation (6).



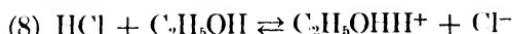
11. When heated ammonia gas is passed over an iron catalyst it breaks down to N<sub>2</sub> and H<sub>2</sub>. Liquid ammonia is the source of hydrogen for atomic hydrogen torches (see p. 30).

12. Electrolytic caustic soda production is attended by the formation of hydrogen (cathode) and chlorine (anode) as by-products. This hydrogen, formerly wasted, is now being utilized. Not infrequently, it is combined with the anodic chlorine to form a very pure hydrogen chloride which is dissolved in water to give a high quality hydrochloric acid.

**Hydrogen-ion Concentration or pH.**—The hydrogen ion (symbol H<sup>+</sup>) is a hydrogen atom with a positive electric charge resulting from the loss of the one and only electron from its outer shell. Strictly speaking, it is a proton. According to modern ideas of ionization of acids it is believed that the hydrogen ion, as such, exists only to a very limited extent in solution because protons cannot exist in polar<sup>1</sup> solvents without combining with the solvent. For example, in aqueous solutions the proton of an acid combines with a molecule of water resulting in the hydronium ion (H<sub>3</sub>O<sup>+</sup>) according to the following reaction (7):



This combination of a proton with solvent is also true of other polar solvents such as alcohol which is of considerable pharmaceutical importance (8).



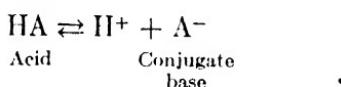
<sup>1</sup> Polar compounds are those in which the centers of negative and positive electricity do not coincide, thus creating an electrical field about the molecule. The molecules may be considered as differentially charged bodies, somewhat similar to small magnets (positive at one end and negative at the other).

However, hydrocarbons such as benzene, etc., are not polar and and are incapable (in an anhydrous form) of accepting protons. They are spoken of as *aprotic* solvents, and acids dissolved in them exist in a wholly undissociated form and do not behave as acids in the usually accepted sense of the word.

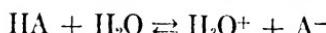
For the sake of simplicity this discussion will be confined to aqueous solutions because they illustrate ionization phenomena as well as any solvent. Thus, to be exact in discussing the ionization of acids in water the hydronium-ion concentration should be spoken of rather than the hydrogen-ion concentration. The hydronium ion characterizes all acids, is responsible for their acidic properties when in aqueous solution, and may be taken as an index of the rate at which a metal will dissolve in the solution, the rate at which cane sugar will be inverted in the acid solution, etc.

The hydroxyl ion (symbol  $\text{OH}^-$ ) is a radical composed of a hydrogen atom, an oxygen atom, and an electron giving the radical a negative electric charge. It is the hydroxyl ion which is responsible for the chemical properties of all alkalies.

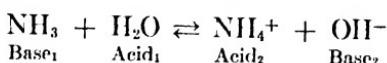
The modern Brönsted-Lowry<sup>1</sup> concept of acids and bases (*i. e.*, "an acid is a substance, molecular or ionic, capable of giving up a proton to another substance, and a base is a substance, ionic or molecular, capable of combining with a proton") is generally accepted as most completely expressing the relationship of acids and bases. Acids ionize according to the following reaction forming a hydrogen ion and a conjugate base:



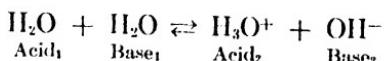
Acids will act as acids only when the solvent has basic properties enabling it to accept the proton as, for instance, water:



Bases will "dissociate" only when the solvent has acidic properties enabling the base to pick up protons. A typical example is ammonia which will combine with the protons liberated by water to give the ammonium ion and the hydroxyl ion as follows:



From the preceding discussion it is apparent that water may act either as an acid or as a base and is therefore spoken of as being amphoteric or amphiprotic. This is illustrated by the equation for the ionization of water:



When 1 molecule of water ionizes as shown above, it forms one

<sup>1</sup> Chem. Rev., 5, 231 (1923).

hydronium ion and one hydroxyl ion. Thus, pure water is always neutral because it contains just as many hydronium ions as hydroxyl ions. If a solution contains a greater number of hydronium ions than hydroxyl ions it is acidic (acid), and if it contains less hydronium ions than hydroxyl ions it is basic (alkaline). There is always a constant relationship between the concentrations (expressed as normality) of the two ions present, namely, the *product of the concentrations is equal to a constant*.

$$C_{H_3O^+} \times C_{OH^-} = K$$

For pure water the constant  $K = (1 \times 10^{-7}) (1 \times 10^{-7}) = 1 \times 10^{-14}$   
 $\left( \frac{1}{100,000,000,000,000} \text{ or } 0.0000000000001 \right)$  at 25° C. Therefore, if one concentration is high the other must necessarily be low in order that the product of the two concentrations will always be the same, namely  $1 \times 10^{-14}$ . For example, if the concentration of  $H_3O^+$  (expressed as  $C_{H_3O^+}$  or  $[H_3O^+]$ ) is  $1 \times 10^{-3}$ , then the concentration of  $OH^-$  ( $C_{OH^-}$  or  $[OH^-]$ ) must be  $1 \times 10^{-11}$  in order to equal the constant.<sup>1</sup> Thus,

$$(1 \times 10^{-3}) (1 \times 10^{-11}) = 1 \times 10^{[-3+(-11)]} = 1 \times 10^{-14} = K.$$

Because of this definite mathematical relationship it can be readily seen that the hydroxyl-ion concentration is being stated indirectly whenever the hydronium-ion concentration is given.

A possible source of confusion in considering hydronium-ion concentration lies in the fact that acids can be and are thought of in two ways:

1. *Total (Titratable) Acidity*.—Expressing acidity in this way simply means that the acid concentration is stated in terms of the amount of the acid substance present in a definite amount of the solution. For example, we may consider 0.1 N solutions of HCl and CH<sub>3</sub>COOH. There is no difference in the total acid concentration of these two solutions. This expression of concentration does not show what portion of the acid is dissociated, but merely the total amount of acid, dissociated and undissociated, that is present. This acidity is commonly expressed in terms of per cent (by weight), Gm. per 100 cc., molarity,<sup>2</sup> molality,<sup>3</sup> or normality.<sup>4</sup> Procedures for the determination of these expressions are known as acidimetry and alkalimetry.

<sup>1</sup> In multiplying two powers of the same number, the exponents are added to get the exponent of the product, and in dividing two powers of the same number the exponent of the divisor is subtracted from the exponent of the dividend to get the exponent of the quotient.

<sup>2</sup> A molar solution contains a gram-molecular weight of the substance in 1000 cc. of solution.

<sup>3</sup> A molal solution contains a gram-molecular weight of the substance in 1000 Gm. of solvent.

<sup>4</sup> A normal solution contains a gram-equivalent weight of substance in 1000 cc. of solution. A gram-equivalent weight of a substance is the gram-molecular weight divided by a number representing the number of gram-atomic weights of hydrogen or its equivalent present in the compound.

2. *Hydronium-ion Concentration.*<sup>1</sup>—This expression of acidity is the one representing the actual acidic "intensity" of a solution which in turn depends upon the amount of hydronium-ion present through dissociation of the acid molecules. Acids are usually spoken of as being "strong" or "weak." The "strong" acids are those which are highly ionized (*e. g.*, HCl, HNO<sub>3</sub>, H<sub>2</sub>SO<sub>4</sub>, etc.), whereas the "weak" acids are those which are ionized only slightly (*e. g.*, HCN, H<sub>3</sub>BO<sub>3</sub>, organic acids, etc.). Therefore, although we find no difference in *total* acidity between 0.1 N HCl and 0.1 N CH<sub>3</sub>COOH, there is a considerable difference in the hydronium-ion concentration because HCl in that concentration is almost completely ionized, and CH<sub>3</sub>COOH is ionized very little. Bases, also, are designated as being "strong" and "weak" depending upon the extent of ionization. Hydronium-ion concentration can be expressed in the same way as total acidity, *e. g.*, as grams of hydronium ion per 100 cc. of solution, or more commonly as gram-equivalents of H<sub>3</sub>O<sup>+</sup> per liter.

The expression of hydronium-ion concentration in aqueous solution is limited by the ionization constant of water to a range of between  $1 \times 10^0$  and  $1 \times 10^{-14}$  (not including the extreme limits). Because the numbers expressing hydronium-ion concentration are mathematically cumbersome to use in expressing acidity, it was suggested by Sörenson that they could be more practicably expressed as negative logarithms to the base 10. This number (the negative log) is called the "hydrogen-ion exponent" and is designated by the symbol pH. Therefore, we have the following relationships:<sup>2</sup>

$$\text{pH} = -\log[\text{H}^+] = -\log[\text{H}_3\text{O}^+] = \log \frac{1}{[\text{H}_3\text{O}^+]}$$

The calculation of pH from the hydronium-ion concentration and *vice versa* offers some difficulty to the average student, usually because of unfamiliarity with logarithmic manipulations. The authors have taught a rather simplified method of calculation for a number of years with considerable success. Briefly, for the conversion of [H<sub>3</sub>O<sup>+</sup>] expressed in normality to pH it consists of the following steps:

1. Obtain the [H<sub>3</sub>O<sup>+</sup>] as gram-equivalents per liter (normality).
  2. Convert the decimal expression of normality to the exponential form (*i. e.*, to a number multiplying a whole number power of 10).
  3. Take the log of the number and add it to the exponent.
  4. Change the sign of the exponent and call it pH.  
(The conversion of pH to [H<sub>3</sub>O<sup>+</sup>] is essentially the converse).
- To illustrate: What is the pH of a solution containing 0.0000343 gram-equivalents of H<sub>3</sub>O<sup>+</sup> per liter?

<sup>1</sup> Often designated as hydrogen-ion concentration but in keeping with the preceding discussion the above nomenclature is preferred.

<sup>2</sup> The reader will note that in agreement with the previous discussion the [H<sub>3</sub>O<sup>+</sup>] is to be considered [H<sup>+</sup>], and, indeed, in *aqueous solutions* it is immaterial whether the expression "hydronium ions" or "hydrogen ions" is used. Exceptions arise only when other solvents are considered.

*Step 1.*

The information is already given, the  $[H_3O^+]$  being 0.0000343 N.

*Step 2.*

$$[H_3O^+] = 0.0000343 \text{ N} = 3.43 \times 10^{-5} \text{ N}$$

*Step 3.*

$$\log 3.43 = 0.54$$

$$\therefore [H_3O^+] = 3.43 \times 10^{-5} = 1 \times 10^{(-5+0.54)} = 1 \times 10^{-4.46}$$

*Step 4.*

$$[H_3O^+] = 1 \times 10^{-4.46}$$

$$\therefore pH = 4.46.$$

To illustrate the conversion of pH to  $[H_3O^+]$ :

Calculate the  $[H_3O^+]$  of a solution having a pH of 11.56.

*Step 1.—Change the sign of the pH and make it a power of 10.*

$$pH = 11.56$$

$$[H_3O^+] = 1 \times 10^{-11.56}$$

*Step 2.—Convert the exponent to a negative whole number and a positive log having a zero characteristic.*

$$[H_3O^+] = 1 \times 10^{-11.56} = 1 \times 10^{(-12+0.44)}$$

*Step 3.—Convert the log to a number and remove from the exponent.*

$$[H_3O^+] = 1 \times 10^{(-12+0.44)} = 2.8 \times 10^{-12}$$

*Step 4.—Convert the exponent form of the number to the decimal form.*

$$[H_3O^+] = 2.8 \times 10^{-12} \text{ N} = 0.000000000028 \text{ N}$$

As further typical examples of the solution of these problems the following may be solved by three methods: (A) the above method, (B) the use of the negative log of  $[H_3O^+]$ , (C) the use of the log of the reciprocal of the  $[H_3O^+]$ .

1. What is the pH of a solution containing 0.00001 gram-equivalents of  $H_3O^+$  per liter?

A.  $[H_3O^+] = 0.00001 \text{ N} = 1 \times 10^{-5}$

$$pH = 5$$

B.  $pH = -\log 0.00001 = -[-5] = 5$

C.  $pH = \log \frac{1}{0.00001} = \log \frac{1}{1 \times 10^{-5}} = \log (1 \times 10^5) = 5$

2. What is the pH of a solution containing  $2.86 \times 10^{-4}$  gram-equivalents of  $H_3O^+$  per liter?

A.  $[H_3O^+] = 2.86 \times 10^{-4} = 1 \times 10^{(-4+0.46)} = 1 \times 10^{-3.54}$

$$pH = 3.54$$

B.  $pH = -\log (2.86 \times 10^{-4}) = -[0.46 + (-4)] = -[-3.54] = 3.54$

C.  $pH = \log \frac{1}{2.86 \times 10^{-4}} = \log \frac{10^4}{2.86} = \log 10^4 - \log 2.86 = 4 - 0.46 = 3.54$

3. What is the hydronium-ion concentration of a solution having a pH of 5.62?

A.  $[H_3O^+] = 1 \times 10^{-5.62} = 1 \times 10^{(-6+0.38)} = 2.4 \times 10^{-6}$

B.  $pH = -\log[H_3O^+]$

$$5.62 = -\log[H_3O^+]$$

$$-5.62 = (-6 + 0.38) = \log[H_3O^+]$$

$$[H_3O^+] = 2.4 \times 10^{-6}$$

C.  $pH = \log \frac{1}{[H_3O^+]}$

$$5.62 = \log \frac{1}{[H_3O^+]}$$

$$= \log 1 - \log[H_3O^+]$$

$$= 0 - \log[H_3O^+] = -\log[H_3O^+], \text{ etc., as in B}$$

4. What is the pH of a 0.1 N solution of NH<sub>4</sub>OH if it is 1.31 per cent ionized?

A. NOTE.—At this point we may introduce a new term, pOH, which is a term expressing the hydroxyl-ion concentration in the same way that pH expresses hydronium-ion concentration. It is easily obtained by subtracting the pH from 14. Therefore:

$$pOH = 14 - pH$$

$$\text{or } pH = 14 - pOH$$

This problem is readily solved by attacking it as a pH problem, but solving for pOH instead and then finally subtracting the pOH from 14 to get the pH.

$$0.1 \text{ N} \times 1.31\% = 0.00131 \text{ N} \text{ (with respect to OH}^-)$$

$$[\text{OH}^-] = 1.31 \times 10^{-3} = 1 \times 10^{(-3+0.12)} = 1 \times 10^{-2.88}$$

$$\therefore pOH = 2.88$$

$$pH = 14 - 2.88 = 11.12$$

B.  $[\text{OH}^-] = 0.1 \text{ N} \times 1.31\% = 0.00131 \text{ N}$

and, since  $[H_3O^+] [\text{OH}^-] = 10^{-14}$

$$[H_3O^+] = \frac{10^{-14}}{[\text{OH}^-]} = \frac{10^{-14}}{0.00131}$$

$$pH = -(\log 10^{-14} - \log 0.00131)$$

$$\log 10^{-14} = -14 = 6-20$$

$$\log 0.00131 = 7.12 - 10$$

$$pH = -[6-20-(7.12-10)] = 11.12$$

C.  $0.1 \text{ N} \times 1.31\% = 0.00131 \text{ N}$ , the OH-ion concentration.

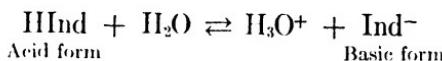
$$10^{-14} \div 0.00131 = 7.63 \times 10^{-12} \text{ N}, \text{ the H}_3\text{O}^+ \text{ concentration.}$$

$$pH = \log \frac{1}{7.63 \times 10^{-12}} = 11.12$$

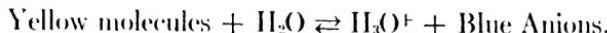
Hydronium-ion concentration can be measured by three greatly different methods: colorimetric, electrometric and chemical.

The colorimetric method utilizes reagents called indicators.

Indicators are usually weak organic acids or bases in which the undissociated molecule has one color, and the anion or cation produced by dissociation has another color. This may be illustrated by considering the ionization of a typical weak acid, bromphenol blue, which exhibits a yellow color in the acid form, and a blue color in the basic form. Representing bromphenol blue by the general formula ( $HInd$ ) for an indicator acid we have:



( )



The law of mass action when applied to the first equation<sup>1</sup> gives us:

$$\frac{[H_3O^+][Ind^-]}{[HInd][H_2O]} = K; \frac{[H_3O^+][Ind^-]}{[HInd]} = K[H_2O]; \frac{[H_3O^+][Ind^-]}{[HInd]} = K,$$

or

$$[\text{H}_3\text{O}^+] = [\text{HIInd}] = [\text{Yellow Molecules}]$$

$$K_1 = \frac{[\text{Ind}^-]}{[\text{Ind}^+]} = \frac{[\text{Blue Anions}]}{[\text{Yellow Molecules}]}$$

From the above mathematical expression it is apparent that since  $K_1$  is constant, the variation of  $[H_3O^+]$  changes the ratio of yellow molecules to blue anions. If the  $[H_3O^+]$  becomes smaller, then the ratio of yellow molecules to blue anions must change so that we have relatively more blue anions than yellow molecules. The reverse would be true if the  $[H_3O^+]$  becomes larger. The qualities desired in an indicator are: that there be a sharp contrast between the two colors and that the color change be effected by a small change of pH. There is a sufficient number of indicators to cover the whole range of hydrogen-ion concentration, with a satisfactory amount of overlapping and duplication.

In the following table is given a number of the more common indicators, together with their respective ranges of pH and color changes.

<i>Indicator</i>	<i>Range of pH and Color Changes</i>
Meta cresol-purple	1.2 (red) to 2.8 (yellow)
Hellige orange	2.6 (red) to 4.2 (yellow)
Bromphenol blue	3.0 (green) to 4.6 (blue)
Methyl orange	3.1 (red) to 4.4 (yellow)
Bromoresol green	4.0 (yellow) to 5.6 (blue)
Methyl red	4.2 (red) to 6.3 (yellow)
Chlorphenol red and bromoresol purple	5.2 (green) to 6.8 (purple)
Bromthymol blue	6.0 (yellow) to 7.6 (blue)
Phenol red	6.8 (yellow) to 8.4 (red)
Cresol red	7.2 (yellow) to 8.8 (red)
Thymol blue	8.0 (yellow) to 9.6 (blue)
Phenolphthalein	8.3 (colorless) to 10.0 (red)
Thymolphthalein	9.4 (colorless) to 10.6 (blue)
Nitro yellow	10.0 (faint yellow) to 11.6 (deep yellow)
Violet	12.0 (purple) to 13.6 (blue)

<sup>1</sup> Since  $H_2O$  is very nearly constant in these solutions, it may be incorporated into the constant  $K$  to give a new constant  $K_1$ .

The technique of measuring pH by the *colorimetric method* involves matching the color of the unknown solution treated with a proper indicator to the colors of solutions of known pH treated

with the same indicator. When the solution of which the pH is to be measured is colored, the color must be duplicated in the comparison solutions of known pH. This is accomplished by putting an equal volume of the solution in the line of the light passing through the standard colors.

Various apparatus have been produced commercially to facilitate the colorimetric measurement of pH. Figures 2 and 3 show two forms of the LaMotte comparators in which the standard colors are supplied in sealed test-tubes. The standard solutions are not permanent and, therefore, must be replaced after a period of time somewhat greater than a year. Figures 4 and 5 show side and front views of the Hellige comparator which uses disks containing little

windows of glass having colors that are exactly the same as the colors of solutions of known pH which have been treated with the



FIG. 2

manent and, therefore, must be replaced after a period of time somewhat greater than a year. Figures 4 and 5 show side and front views of the Hellige comparator which uses disks containing little windows of glass having colors that are exactly the same as the colors of solutions of known pH which have been treated with the



FIG. 3

indicators corresponding to the particular color disk. One of the disks is also shown. These standard disks have the advantage of being permanent. Figure 6 shows a block containing a sufficient number of indicators to cover a considerable portion of the pH range. The colorimetric method of measuring pH is widely used

in industry. For convenience, the colorimetric method of determining hydrogen-ion concentration has been adopted for pharmaceutical purposes and is to be employed where pigments and proteins present in the solution do not vitiate its use.

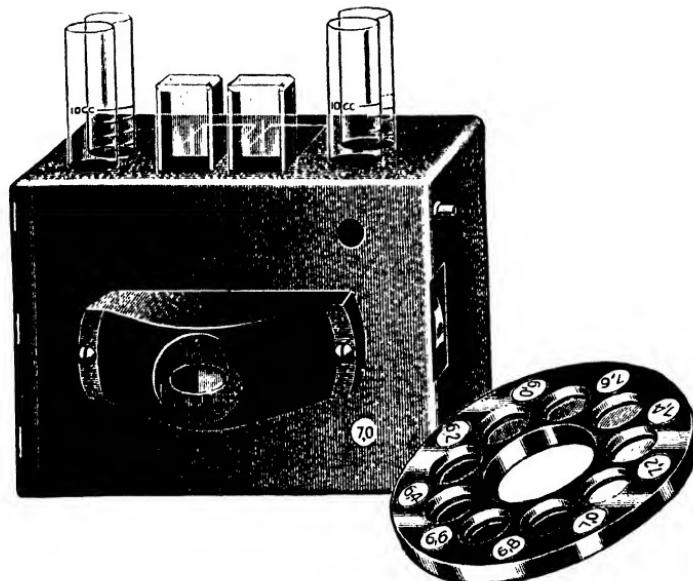


FIG. 4



FIG. 5

The *electrometric or potentiometric method* is based upon the measurement of the voltage developed between special electrodes when immersed in the solution. The difference in potential is measured with a potentiometer and since this difference is directly dependent upon the presence of  $\text{H}_3\text{O}^+$  in the solution, it is equivalent to determining the concentration of  $\text{H}_3\text{O}^+$ . The voltmeter, or its equivalent,

is frequently graduated to read directly in pH on instruments designed specifically for this purpose (Fig. 7). The electrometric method is increasing in importance because it is rapid, can be used in solutions containing pigments and proteins, and because it can be used, with the aid of relays, to control a chemical reaction in which the pH must be carefully established and maintained. (See



FIG. 6

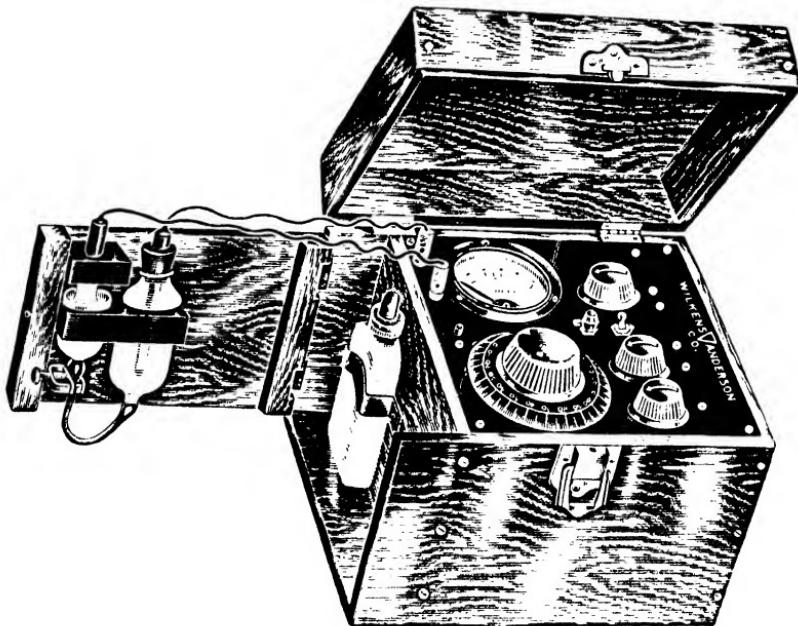


FIG. 7

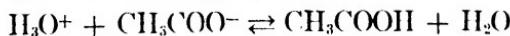
brochure on pH measurements published by American Society for Testing Materials, 1916 Race Street, Philadelphia, 3, Pa.)

The *chemical method* for measuring hydrogen-ion concentration is only of scientific interest and is not used practically as a method for determining pH. It is impractical because it involves the addition of chemicals to the solution of unknown pH and which by themselves, change the hydrogen-ion concentration of the solution. One means of determining pH chemically is to compare the rate of inversion of sucrose with the rate at which an acid of known hydrogen-ion concentration inverts the sucrose under the same conditions. This particular reaction is convenient because the inversion of the sucrose can be measured in a polariscope.

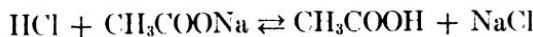
In addition to the three well-defined, exact methods of pH determination, there is a less exact but more practical variation of the colorimetric method in which strips of paper are impregnated with an indicator. Merely dipping the paper in the unknown solution produces a color on the paper which can be compared with charts supplied by the manufacturer. These are of value to diabetic patients for testing the actual acidity of the urine, and also to the chemist and pharmacist. Examples of these papers are the "Nitrazine" paper (Squibb), "pHydrion" paper (Central Scientific Co.), "Alkaacid Test Ribbon" (Fisher Scientific Co.), and "Universal pH Indicator Paper" (Braun-Knecht-Heimann Co.).

The importance of controlling the pH in solutions has been recognized for a long time. Unfortunately, the pH of a solution, even when carefully adjusted, will not remain at that point indefinitely because of extraneous factors such as alkali in the glass from which cheap bottles are made,  $\text{CO}_2$  in the air, etc. To remedy this situation, use is made of *buffer mixtures*. A buffer mixture (or *buffer pair*) is usually a solution composed of a weak acid and a salt of the weak acid or a weak base and its salt. The latter is not widely used because of greater sensitivity to temperature changes. A buffered solution will resist any great change in the pH which may be caused by the addition of small amounts of acids or bases.

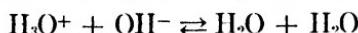
As an example, a typical acetic acid-sodium acetate buffer mixture will clearly show the mechanism of buffering. Upon the addition of HCl to a buffer of this composition we have the introduction of potentially enough hydronium ions to change the pH tremendously. However, in the buffer we have acetate ions (furnished by the sodium acetate) which are strong bases and are capable of combining with the hydronium ion to form relatively non-ionized acetic acid molecules. This effectively removes the acidic hydronium ions and prevents them from exerting their activity. In effect, we have converted a "strong" acid to a "weak" acid according to the following equations:



or written molecularly,



Addition of an alkali, such as NaOH, to this buffer mixture sets up a different chain of events to take care of the excess hydroxyl ions. The acetic acid in the buffer mixture, while not greatly ionized, furnishes enough hydronium ions to combine with the added hydroxyl ion to form water, which is practically non-ionized insofar as affecting the pH is concerned. This is illustrated by the following reactions:



or written molecularly,



The adjustment and stabilization of pH in solutions is of widespread importance in many fields of work. In pharmacy the close control of pH in many pharmaceutical preparations is of utmost concern. The stability of preparations such as tinctures of aconite and digitalis, fluidextract of ergot, and others is dependent upon adjustment of the pH to a relatively acidic reading, because the deterioration of these preparations is greatly accelerated under alkaline conditions. Aqueous and dilute alcoholic solutions of most of the vitamin B group, particularly thiamine hydrochloride, are sensitive to a pH over 5 and for maximum stability should have a pH ranging from 3.5 to 4.5. Solutions of alkaloidal salts should be kept on the acid side of the pH scale to prevent precipitation of the free alkaloid. Maintenance of a good coloration in many galenical preparations is dependent upon the control of pH. It is important to note that certain drugs used in prescription work may be unstable in either acidic or alkaline media. Among the common drugs affected, Wyss<sup>1</sup> lists the following:

<i>Alkali Unstable</i>	<i>Acid Unstable</i>
Acetanilid	Diluted HCN
Acetophenetidin	Salts of Organic Acids
Chloral Hydrate	Arsphenamine
Phenobarbital and other barbiturates	Diphenyl Hydantoin Sodium (Dilantin Sodium)
Guaiacol Compounds	Pancreatin
Hydrogen Peroxide	Paraldehyde
Mercuric Chloride	Sodium Nitrite
Mercurous Chloride	Sodium Thiosulfate
Strophanthin	
Peptin	
Pepsin	
Resorcinol	
Resorcinol Mono-acetate	
Salol	
Santonin	
Tannic Acid	
	<i>Acid and Alkali Unstable</i>
	Acetylsalicylic Acid
	Antipyrine
	Atropine
	Creosote Carbonate

The adjustment of pH in prescriptions is carried out by the following practical method.<sup>1</sup>

<sup>1</sup> Wyss, A. P., *The Importance of pH in Prescriptions*, Merck Report, p. 16, April, 1945.

**Practical Adjustment of pH.**—“*Step I.*—The prescription ingredients are combined and the preparation is brought to within  $\frac{1}{2}$  to 1 fluid ounce of the desired volume. Using an indicator paper of wide pH range, the approximate pH value of the mixture is determined by moistening the paper with a drop of the preparation and comparing the resulting color with the standards provided. This step serves to indicate whether acid or alkali will be needed for the adjustment and to show approximately how far the pH of the mixture is from the desired range.

*Step II.*—Small pieces of indicator paper, especially suitable for showing differences of pH over a narrow range of pH, then are placed on a pill tile or other convenient surface. Let it be assumed, for example, that the desired pH is to be approximately 4, with an upper limit of 5 and a lower limit of 3. A drop of each of three standard buffer solutions is placed on individual pieces of the indicator paper—one buffer solution representing the upper limit of the desired pH range (pH 5), one the lower limit (pH 3), and one the median value (pH 4). The colors thus produced will serve as guides in adjusting the pH of the finished prescription.

*Step III.*—Dilute hydrochloric acid or sodium hydroxide of known strength is added in measured small amounts to exactly 10 cc. of the prescribed mixture as the case requires. Each addition is followed by thorough mixing and testing on fresh portions of indicator paper until the color obtained shows the pH of the sample to compare favorably with that produced by the specified standard buffer solution (pH 4). From the amount of acid (or alkali) required for the 10 cc. portion of the prescribed mixture, the volume needed for the remainder of the prescription may be calculated.

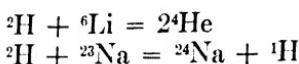
*Step IV.*—The calculated volume of acid (or alkali) is combined with the rest of the mixture, the above portion which was subjected to the preliminary adjustment is added, and sufficient vehicle is used to yield the final volume. The completed preparation is mixed thoroughly and subjected to a final check of the pH value; if satisfactory, the product is packaged properly and labeled, with complete instructions to the patient concerning proper conditions of storage and use.”

**Isotopes of Hydrogen.**—Two isotopes<sup>1</sup> of hydrogen occur in Nature, these having mass 1 and 2. Of these, <sup>1</sup>H is by far the most abundant. <sup>2</sup>H (known as Deuterium) is estimated to be present in ordinary hydrogen in the concentration of about 1 part in 5000.

Because of the fact that its vapor pressure in the liquid phase is slightly lower than that of liquefied hydrogen (<sup>1</sup>H), deuterium lends itself to concentration and, by the application of this property, Prof. H. C. Urey of Columbia University succeeded in isolating a small quantity of the pure isotope by the careful fractional distillation of liquid hydrogen. Most of the pure isotope which is

<sup>1</sup> An isotope is one of several possible forms of an element, all forms having identical chemical properties but different atomic weights.

produced at the present time is used in experiments dealing with the bombardment of molecular nuclei, and some very interesting results have been obtained. For example:



The isotope of sodium ( ${}^{24}\text{Na}$ ) produced in the last reaction is said to be radioactive for a period of about fifteen hours. Salts of this radioactive sodium have been made and there is the possibility that they may be administered internally. (See p. 659.)

Just how the introduction of one or more atoms of deuterium into a molecule will affect the therapeutic activity of the resulting substance has not been determined, but it is predicted that these substances will be influenced markedly by the presence of this atom.

**Deuterium Oxide (Heavy Water).**—Pure deuterium oxide may be prepared by burning pure deuterium in oxygen or by the electrolysis of ordinary water. In the latter method the water which contains hydrogen with mass 1 is broken down first and the hydrogen and oxygen are liberated at the electrodes (nickel electrodes 0.5 molar sodium hydroxide as electrolyte—Taylor). As this process is allowed to continue the per cent of deuterium oxide ( $\text{D}_2\text{O}$ ) in the water becomes greater and greater and thus it is possible to obtain almost pure  $\text{D}_2\text{O}$ . This method was proposed by Urey and was used by G. N. Lewis of California in the preparation of "Heavy Water," the physical constants of which are reported to be:

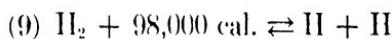
1. Density, 1.1059 at  $20^\circ\text{C}$ .
2. Freezing-point,  $3.82^\circ\text{C}$ .
3. Boiling-point,  $101.42^\circ\text{C}$ .
4. Heat of fusion, 1510 calories.
5. Heat of vaporization at  $25^\circ\text{C}$ ., 10,743 calories.
6. Temperature of maximum density,  $11.6^\circ\text{C}$ .
7. It is about 25 per cent more viscous than ordinary water.
8. Salts are about 10 per cent less soluble in it than they are in ordinary water.
9. Salts dissolved in heavy water are ionized to a lesser degree than when dissolved in ordinary water.

The facts that certain seeds failed to germinate and that tadpoles and guppies could not live when placed in heavy water gave rise to the supposition that this form of water was toxic to all forms of life. In an attempt to prove or disprove its toxicity a number of persons have drunk variable quantities of this water each day for varying lengths of time and, to date, no untoward results have been recorded. If, as is indicated by the results of these experiments, this water is not toxic to human beings then some other explanation for its toxicity to seeds and lower forms of life must be made. It is possible that this may be attributed to the same phenomenon which causes certain seeds to sprout and grow better in water obtained from melting ice than they will in water which is obtained by condensing steam.

Methods have been developed for the detection of minute amounts of D<sub>2</sub>O in ordinary water. This has made it possible to use it as a *tracer compound* in chemical and physiological compounds.

**Uses.** - Hydrogen is used in the Haber process for nitrogen fixation (*q. v.*), for inflating balloons; for the production of high temperatures when burned with oxygen; and for the hydrogenation of oils used for edible and other purposes.

The work of Dr. Irwin Langmuir of the General Electric Company made it possible to obtain one of the highest temperatures ever produced and also to effect a weld in a reducing atmosphere. Hydrogen is passed through an electric arc wherein molecular hydrogen is converted into atomic hydrogen (9). Immediately upon issuing from the arc the atomic hydrogen combines to form molecular hydrogen and a tremendous quantity of heat is evolved. This hydrogen then burns with the oxygen of the air. In short, the flame consists of a nucleus of combining hydrogen atoms surrounded by a shell of burning molecular hydrogen. A temperature of about 5000° C. has been obtained.



Other than its use in the activated state as a laboratory agent in the preparation of many chemical compounds (see Reduced Iron p. 610), it is never used in pharmacy or medicine.

## CHAPTER III

### WATER AND HYDROGEN PEROXIDE

#### WATER

Formula, H<sub>2</sub>O. Molecular Weight, 18.016

**History.**—The nature of water was held to be elementary until the latter part of the eighteenth century. In Robert Boyle's time (1627–1691) it was known that some metals, *e. g.*, tin, iron, zinc, etc., dissolved in aqueous solutions of hydrogen chloride with the evolution of a vile-smelling gas, which was thought to be air contaminated with "obnoxious oils." This view was held by all chemists until 1781, when Cavendish showed that the evolved gas could be purified of its odor and then possessed constant physical and chemical properties differing widely from those of air. He not only demonstrated that this gas burned in air with the evolution of heat and the formation of water, but also determined the quantitative relations and found that it took nearly 1000 volumes of air to burn 423 volumes of "hydrogen" gas. This important discovery was confirmed by the subsequent experiments of Humboldt and Gay-Lussac. In 1783 Lavoisier decomposed water into its elements and showed that it was composed of about 1 part by weight of hydrogen and about 8 parts by weight of oxygen. It was not until 1805 that Gay-Lussac and Humboldt proved the volume composition of water.

**Occurrence.**—The ocean is by far the most abundant of all natural sources of water. About 25 per cent of the water vapor rising therefrom is condensed to rain, snow, sleet, etc., and precipitated on the land. In this way lakes and rivers are formed; or the water is absorbed by the soil and used by plant life; or, perhaps, it reappears again in springs, etc. *Mineral waters* are natural spring or well waters which contain in solution sufficient quantities of mineral or gaseous matter to render them unfit for domestic use. The nature and quantity of the dissolved substances make these waters of more or less value as medicinal agents. The Council on Pharmacy and Chemistry of the American Medical Association has this to say about the therapeutic values of mineral waters: "The Council has declared artificial mineral waters to be non-essential modifications of natural waters, that natural mineral waters are only one feature prescribed by spas and health resorts and that mineral waters are not eligible for consideration for acceptance as individual products, since there is no convincing evidence to show that the many therapeutic claims which are made for these preparations as bottled for individual use are valid." They are usually designated

according to the character of their most important medicinal constituent. Thus:

*Alkaline waters* usually contain appreciable quantities of sodium and magnesium sulfates together with some sodium bicarbonate. Apollinaris, Vichy and the waters from the Capon Springs (W. Va.) are examples.

*Carbonated waters* are those which have been charged while in the earth with carbon dioxide under pressure. They usually effervesce on coming to the surface. Such waters contain calcium and magnesium carbonates in solution as bicarbonates. Springs in Colorado and Yellowstone Park (Wyoming) yield waters of this class. Artificial carbonated waters may be made by charging water under pressure with carbon dioxide.

*Chalybeate waters* contain iron in solution or in suspension and are characterized by a ferruginous taste. Upon exposure to the atmosphere the iron is usually precipitated as hydroxide or oxide. Spring and well waters containing iron are very common.

*Lithia waters*, as a rule, do not contain appreciable quantities of lithium. If present, it occurs in the form of the carbonate or chloride.

*Saline waters* are sometimes called "purgative waters" and contain relatively large amounts of magnesium and sodium sulfates with sodium chloride. The waters from springs located at Saratoga Springs, N. Y., and from the Blue Lick Springs in Kentucky are examples.

*Sulfur waters* contain hydrogen sulfide. These waters, *e. g.*, the waters from White Sulphur Springs, W. Va., Richfield Springs, N. Y., etc., deposit sulfur upon exposure to the atmosphere.

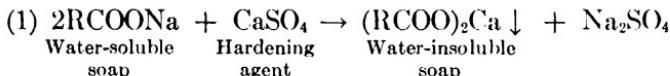
*Siliceous waters* occur in Yellowstone Park and Iceland and contain very small quantities of soluble alkali silicates.

Water constitutes from 75 to 90 per cent of green plants; from 80 to 98 per cent of fruits; and about 65 per cent of the animal body. In the form of water of hydration it enters into the composition of many chemicals.

**Physical Properties.**—Pure water is a tasteless, odorless, limpid liquid which is colorless in small quantities but greenish-blue in deep layers. It is only slightly compressible and is a poor conductor of heat and electricity. At atmospheric pressure (760 mm.) water exists as a liquid between 0° and 100° C., reaching its greatest density at 4° C. Below 0° C. it becomes a solid and above 100° C. a vapor. When water passes from one physical state to that of another, heat (energy) is either consumed or liberated. Thus, when 1 Gm. of ice at 0° C. changes to 1 Gm. of water at 0° C., 79.71 calories of heat are required to effect the transformation (heat of fusion of ice). Likewise, when 1 Gm. of water at 100° C. turns to 1 Gm. of steam at 100° C., 539.55 calories of heat are consumed (heat of vaporization). These temperatures are known as melting- or freezing-point (solids to liquids or *vice versa*) and as boiling-point (liquids to vapors), respectively. The boiling-point of a liquid is that temperature at which the pressure of its saturated vapor is equal to the

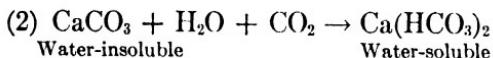
standard atmospheric pressure (760 mm.). The *specific heat* of a substance is that quantity of heat expressed in calories required to raise 1 Gm. of it  $1^{\circ}$  C. The specific heat of water at  $14.5^{\circ}$  C. is 1. The unit quantity of heat is called the *calorie* (cal.). It is the amount of heat required to raise 1 Gm. of water at  $14.5^{\circ}$  C. to a temperature of  $15.5^{\circ}$  C. The large calorie, or kilocalorie, is 1000 times larger than the calorie.

The dissolved impurities in all ordinary potable waters amount to very little, usually less than 0.1 of 1 per cent. One of the chief factors that determines the value of a water for domestic and commercial purposes is its hardness. This property is occasioned by the presence in solution of varying amounts of calcium, iron and magnesium salts, which convert the ordinary soap (water-soluble sodium and/or potassium salts of high molecular weight fatty acids) into water-insoluble calcium, iron, and/or magnesium salts of the fatty acids (1).



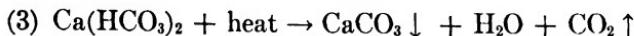
Only when all of the hardening substances have been precipitated as a water-insoluble curd by the above mechanism will the soap begin to lather. It is apparent that hard water may be undesirable in many respects and, therefore, methods of removing hardness have received much attention. Water may possess *temporary* or *permanent* hardness or both.

*Temporary hardness* is caused by the presence in the water of soluble calcium or magnesium bicarbonates. These bicarbonates are formed by the action of water charged with carbon dioxide percolating through limestone deposits to cause the following reaction to take place (2).



Temporarily hard water may be "softened" by the following procedures:

1. *Boiling*.—The carbon dioxide that has held the insoluble calcium and magnesium carbonates in solution as bicarbonates is driven off by boiling and the insoluble normal carbonate is precipitated (3).



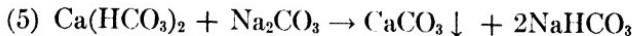
This method, of course, is not too satisfactory when large volumes of "softened" water are needed.

2. *Clark's Lime Process*.—Clark, in 1841, suggested that slaked lime, in quantities just sufficient to react with the bicarbonate ion, be added to the water, thus precipitating the normal carbonate (4).



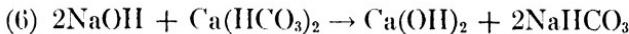
Care must be taken not to add too much slaked lime since this will impart a new hardness to the water which is more difficult to remove than the original.

3. *Addition of Soluble Alkali Carbonates or Hydroxides.*—Sodium carbonate, for example, when added to temporarily hard water will precipitate the normal carbonate (5).

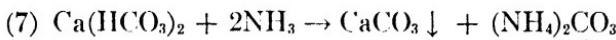


This manner of softening water is familiar to the housewife through the use of *washing soda* ( $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$ ) as a water softener in the laundry.

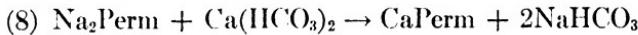
By furnishing hydroxyl ions, sodium hydroxide, on the other hand, converts the bicarbonates to slaked lime (6) which reacts with the calcium or magnesium bicarbonate still remaining (4).



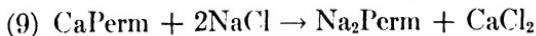
4. *Addition of Ammonia.*—Household ammonia is also used for softening water (7).



5. *Permutit Process.*—An artificial zeolite, called *permutit*, was introduced by Gans (1910) as a means of softening both temporarily and permanently hard waters. Permutit makes use of an ion-exchange reaction for softening water. It is a sodium aluminum silicate (said to be  $\text{Na}_2\text{H}_6\text{Al}_2\text{Si}_2\text{O}_{11}$ ), and may be simply represented by the symbol,  $\text{Na}_2\text{Perm}$ . By passing the hard water through the permutit, an exchange of the "water-hardening" cations is made for "non-hardening" sodium ions (8).

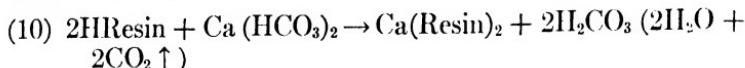


When the permutit is all converted to the CaPerm form it obviously can no longer furnish sodium ions. To restore its activity a strong solution of sodium chloride is allowed to flow through the inactivated permutit, converting it to the sodium form again (9).



6. *De-ionization of Water.*—The latest method for softening both types of water is an outgrowth of the desire to obtain water approximating distilled water in purity without going through the wasteful and expensive distillation procedure. Practically all of the procedures previously mentioned leave some chemical in the water, although the water may be "softened" in the ordinary sense of the word. The presence of salts in water is undesirable in many manufacturing processes. The development of commercial *resinous-ion exchangers* in 1935 made possible the removal of both cations and anions from water. The removal of salts from water by this process consists of two steps. The *first step* is a removal of the cations by passing the water through a *hydrogen-exchange resin*

(HResin) which converts any salt to the corresponding acid by giving up a hydrogen ion in exchange for the metal ion (10).



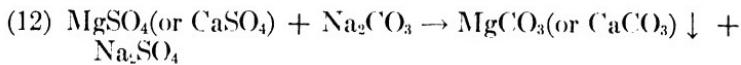
So effectively is the salt changed to the corresponding acid that a "salt machine" has been devised,<sup>1</sup> whereby a sample of water is poured through the resin and the effluvate titrated with standard alkali to determine its acid content. Knowing the stoichiometric relationship between a salt and the acid which it forms, the concentration of salt in the original water can be determined. The results agree very closely with those obtained by gravimetric procedures. The *second step* accomplishes the removal of all anions (now in the form of acids) by passage of the water through another resin (usually an amine-formaldehyde resin) whereby the  $-\text{NHH}_2$  groups neutralize the acids (11).



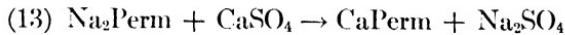
The water which finally issues from the de-ionizer compares very favorably with distilled water in purity and it can be produced at a lower cost.

*Permanent hardness* is caused by the presence in solution of the sulfates, chlorides or hydroxides of calcium or magnesium. These objectionable salts cannot be removed by boiling or by lime treatment of the water. Permanently hard water may be softened by the following procedures.

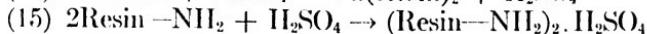
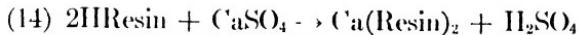
1. *Addition of Soluble Carbonates*.—By adding soluble carbonates (*e. g.*,  $\text{Na}_2\text{CO}_3$ ) to the hard water the insoluble carbonates of calcium and magnesium are precipitated (12).



2. *Permutit Process*.—As previously indicated, this process applies equally well to temporarily and permanently hard waters (13).



3. *De-ionization of Water*.—The resinous-ion exchangers also soften both types of water, inasmuch as all anions and cations are removed irrespective of the salts. The removal of  $\text{CaSO}_4$  from permanently hard water is carried out by the typical two-step mechanism (14) (15).



It is interesting to note that during World War II the resinous-ion exchangers were used as a source of drinking water on life rafts.

The hardness of water is variously expressed. On Clark's scale (English) it is the number of grains of calcium carbonate per

<sup>1</sup> Ion-exchange Resins, Ind. and Eng. Chem., **35**, 859 (1943).

gallon of 70,000 grains of water; in Germany, it is expressed as the number of parts of calcium oxide per 100,000 parts of water; and in France as the number of parts of calcium carbonate per 100,000 parts of water. In the United States, hardness is represented as 1 part of calcium carbonate or its equivalent in 1,000,000 parts of water (1 milligram per liter). Hardness is determined by shaking a measured quantity of the sample of water with gradually added portions of a soap solution (standardized against known calcium chloride solution) until a permanent lather is produced.

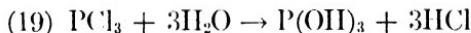
**Chemical Properties.**—In most chemical reactions, water plays merely a mechanical part, *viz.*, that of a solvent for reacting substances. Nevertheless, this relatively stable substance does possess certain well-defined chemical properties which are exhibited on certain occasions. For example, it combines with many oxides to form acids and bases (16 and 17);



it unites with many salts to form hydrates (18);



and it also reacts chemically with some substances in such a manner that double decomposition (metathesis) takes place (19). Such an interaction is called hydrolysis.



A mere trace of moisture very often exerts what is thought to be a catalytic influence upon many chemical changes. For example, perfectly dry hydrogen and oxygen cannot be made to unite when exposed to the action of an electric spark. However, under like conditions, a trace of moisture causes them to combine with explosive violence.

**Recognition of Water by U. S. P. XIII and N. F. VIII With Tests for Purity.**—The U. S. P. XIII recognizes WATER (Aqua), DISTILLED WATER (Aqua Destillata), STERILE DISTILLED WATER (Aqua Des-tillata Sterilis) and WATER FOR INJECTION (Aqua Pro Injectione).—The National Formulary VII recognized REDISTILLED WATER (Aqua Redestillata) and, in addition, gave specifications for Ampul Water.

1. WATER (Aqua) ( $\text{H}_2\text{O}$ ), U. S. P. XIII, must conform to the following requirements and tests: It is a clear, colorless, practically tasteless and odorless liquid.

It should have a range of hydrogen-ion concentration corresponding to a pH of not less than 5.6 and not more than 8.3. The limit of the former may be determined by adding 2 drops of methyl red pH indicator (transition interval, 4.2 [red] to 6.3 [yellow] pH) to 10 cc. of water contained in a clean test-tube. No red color should be produced. The latter limit may be determined by adding 2 drops of phenolphthalein T.S. (transition interval, 8.3 [colorless] to 10.0

[red] pH) to another 10 cc. portion of water contained in a clean test-tube. No pink or red color should develop.

When heated nearly to the boiling-point and agitated, water should not evolve a disagreeable odor. The soluble impurities should not exceed 100 mg. per 100 cc.

Dissolved carbon dioxide in water attacks untarnished lead, copper and some other heavy metal surfaces and forms soluble bicarbonates which may be poisonous. Therefore, the limit of the amount of heavy metals present in Water is specified and tested for as follows: 1 cc. of diluted acetic acid and then 10 cc. of freshly prepared hydrogen sulfide T.S. are added to 40 cc. of Water, heated to 50° C., and allowed to stand for ten minutes. The color of the liquid when viewed downward over a white surface is no darker than the color of a mixture of 40 cc. of the same Water with 10 cc. of distilled water using matched Nessler tubes for the comparison.

The limit of soluble zinc salts is tested for as follows: 3 drops of glacial acetic acid, then 0.5 cc. of potassium ferrocyanide T.S. are added to 50 cc. of Water contained in a glass tube. The solution should not show more turbidity than that produced by 50 cc. of distilled water in a similar glass tube, treated in the same manner, and viewed downward over a dark surface (20).



The U. S. P. XIII requires that Water meet the standards for freedom from *coliform organisms* required for potable water by the United States Public Health Service.

2. DISTILLED WATER, U. S. P. XIII (Aqua Destillata), is defined as "water purified by distillation." The present revision of the U. S. Pharmacopœia does not include a method for its preparation.

Official distilled water is described as "a colorless, clear liquid, without odor or taste." It should have a pH of not less than 5.0, as determined by no red color developing when 2 cc. of neutral methyl red pH indicator is added to 10 cc. of Distilled Water contained in a test-tube. Also, it should have a pH of not more than 7.0 as evidenced by no blue color being produced when 5 drops of bromthymol blue pH indicator (transition interval, 6.0 [yellow] to 7.6 [blue] pH) added to 10 cc. of Distilled Water. One hundred cubic centimeters of Distilled Water when evaporated on a water-bath and dried to constant weight at 100° C., should not leave a residue weighing more than 1 mg. Distilled Water should not respond to appropriate limit tests for sulfate, chloride, calcium, ammonia, carbon dioxide, heavy metals and oxidizable substances (see U. S. Pharmacopœia XIII, p. 600). When Distilled Water is allowed to stand, minute stringy or flocculent particles occasionally make their appearance. These particles are microscopic plants (*confervæ*) developed from spores which have fallen into the distilled water. They may be minimized or entirely prevented by allowing only air that has been passed through a pledge of cotton, to come in contact with the distilled water.

3. STERILE DISTILLED WATER, U. S. P. XIII (Aqua Destillata Sterilis) is prepared by placing Distilled Water in suitable containers, properly closing and sealing them, and then sterilizing preferably by Process C. (See U. S. P. XIII, p. 692.)

Sterile Distilled Water and Distilled Water are not to be used for parenteral administration or in preparations to be used parenterally. For such purposes Water for Injection should be used.

4. WATER FOR INJECTION, U. S. P. XIII (Aqua Pro Injectione).—This product must be dispensed whenever "sterile water" or "sterile distilled water" for parenteral use is required or is dispensed as a vehicle, solvent, or diluent for substances to be administered parenterally. This water is distilled and collected in clean (preferably sterile) containers which have been rinsed with Water for Injection or with freshly distilled water. This water may be used for parenteral solutions immediately, following suitable treatment, or it may be kept overnight at temperatures preventing bacterial growth or deterioration. In addition, it may be packaged and sterilized for future use, the product thus packaged being required to meet certain specifications as to sterility and clarity. It is not permissible to use any bacteriostatic or preservative agents in Water for Injection. This water must be free of pyrogenic substances as specified under the Pyrogen Test, U. S. P. XIII, page 679.

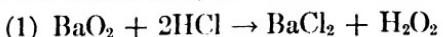
The N. F. VII described a "Redistilled Water." It was deleted from the N. F. VIII because it served no useful purpose, and was more or less replaced by "Water for Injection" (U. S. P. XIII). It has been noted that with a less stringent requirement, the test for oxidizable substances, formerly in the monograph for "Redistilled Water," now appears as a new requirement for "Distilled Water" (U. S. P. XIII).

*Medicinal Uses.*—Water in its several official forms plays an important part in pharmaceutical and medical practice. The specification for Water insures water of a reasonable purity for allaying thirst and for bathing purposes. In addition, when water is taken internally in large quantities it assists in the elimination through the kidneys of impurities in the body by its diuretic effect. In such a capacity, it exercises a decided medicinal influence upon those conditions caused by perverted metabolism. Distilled Water, of course, is universally used in prescription work calling for water as a solvent because of its freedom from chemical impurities. Sterile Distilled Water is suitable for rinsing surgical incisions, instruments, etc., and for other topical applications. Water for Injection, as the name implies, is the vehicle for parenteral injections requiring water as a solvent.

### HYDROGEN PEROXIDE

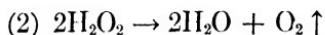
Formula,  $H_2O_2$ . Molecular Weight, 34.02

**History.**—Hydrogen dioxide was discovered by L. J. Thenard in 1818 and he designated it as "oxygenated water." He prepared it by the action of hydrochloric acid on barium peroxide (1).



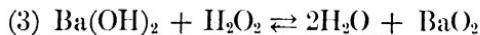
**Occurrence.**—Because of its instability, hydrogen dioxide is found occurring naturally only in very small quantities in air, dew, rain, and snow.

**Physical Properties.**—Pure (100 per cent) hydrogen dioxide is a colorless, astringent, syrupy liquid having a specific gravity of 1.4631 (0° C.). Even at a temperature as low as 20° C., pure hydrogen dioxide will decompose slowly. When heated to 100° C. it decomposes with explosive violence to form water and oxygen (2).

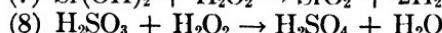
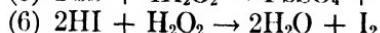
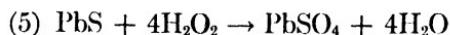


It may be separated with very little decomposition from its aqueous solutions by fractional distillation under reduced pressure. When a concentrated solution (96 per cent) of hydrogen dioxide is cooled to 10° C., colorless, transparent, prismatic crystals separate out. These crystals melt at -1.7° C. Cryoscopic determinations show its molecular weight to be 34.016 and its formula  $\text{H}_2\text{O}_2$ . At ordinary temperatures hydrogen dioxide is miscible in all proportions with water, alcohol and ether. It is more soluble in ether than in water and, therefore, may be extracted from its aqueous solution by shaking the two liquids in a separatory funnel.

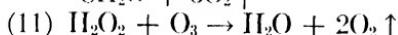
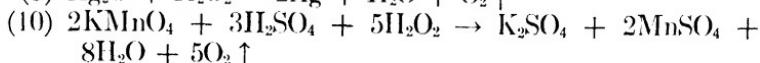
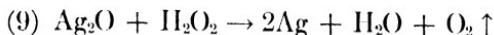
**Chemical Properties.**—Hydrogen dioxide in aqueous solution is a feeble acid and as such enters readily into double decomposition to form peroxides (peroxides or salts of hydrogen peroxide), which easily become hydrated and appear as crystalline precipitates (3 and 4).



When powdered metals, manganese dioxide, charcoal or organic compounds are added to an aqueous solution of hydrogen dioxide, decomposition into water and free oxygen takes place with the evolution of 23,100 calories of heat. This is due to their catalytic action. Alkalies and most salts have a similar action upon hydrogen dioxide. The fact that hydrogen dioxide contains a large amount of internal energy and liberates oxygen when it decomposes, indicates that it is a much more active oxidizing agent than is free oxygen. Thus, in the presence of dilute aqueous solutions of hydrogen dioxide, lead sulfide is converted into lead sulfate (5); iodine is liberated from solutions of hydrogen iodide (6); the hydroxides of the alkaline earth metals are converted into hydrated peroxides (7); and sulfurous acid is oxidized to sulfuric acid (8). Hydrogen dioxide changes some organic coloring agents into colorless compounds and, therefore, is used for bleaching hair, fabrics, etc.



Hydrogen dioxide acts also as a reducing agent. Silver oxide is reduced with a rapid evolution of oxygen (9); potassium permanganate, in acid ( $H_2SO_4$ ) solution, is rapidly changed to manganese sulfate, potassium sulfate and oxygen (10); and both hydrogen dioxide and ozone are reduced when they interact (11). In general, hydrogen dioxide acts as a reducing agent usually with those metallic oxides which easily lose all or part of their oxygen, *e. g.*,  $Ag_2O$ .



**Official Tests for Identity.**—1. When 1 cc. of a solution of hydrogen dioxide is shaken with 10 cc. of distilled water containing 1 drop of diluted sulfuric acid, and then 2 cc. of ether and a drop of potassium dichromate test solution added, an evanescent blue color will appear in the aqueous layer. The color may be transferred to the ether layer by shaking the liquid and allowing it to stand. When sulfuric acid acts upon potassium dichromate, dichromic acid and potassium sulfate are formed (12).



The dichromic acid then reacts with the hydrogen dioxide to form a perchromic acid, thought to have the formula  $(HO)_2Cr(OOH)_3$  (blue color). This perchromic acid is more soluble in ether than in water and in ethereal solution the blue color is much more permanent.

2. When a solution of hydrogen dioxide is added to a mixture of a diluted tincture of guaiac and malt infusion, a blue color is produced.

3. For characteristic oxidation and reduction reactions of hydrogen dioxide, see Chemical Properties, p. 56.

**Commercial Manufacture.**—The commercial manufacture of hydrogen peroxide was influenced greatly by World War II. The most significant progress was not made in methods of synthesis, but rather in the large scale methods for concentrating hydrogen peroxide by distillation under reduced pressure. Solutions containing 35 per cent of  $H_2O_2$  were the highest concentrations available in commercial quantities previous to the war, but now it is possible to obtain 80 to 90 per cent concentrations manufactured by methods developed by German engineers under the stress of the war. Certain pre-war technical developments, *i. e.*, the perfection of corrosion resistant stainless steels by Krupp and the development of special resins suitable for gaskets and tubing, made it possible for Germany to produce highly concentrated peroxide during the war. Because of the explosive instability of hydrogen peroxide in strong solutions, previous attempts to produce such solutions in commercial quantities had proved impractical. In addition to finding methods of concentrating hydrogen peroxide solutions, the Germans also investigated conditions of storing them. It was found that for practical purposes, aluminum (at least 99.5 per cent pure) tank

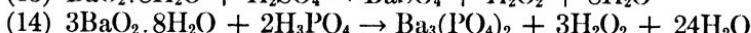
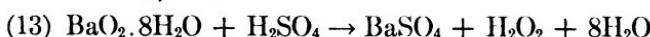
cars and storage tanks were the best to maintain maximum stability. For example, 80 per cent peroxide solutions stored in aluminum tanks under ordinary outside climatic conditions were found to lose less than 1 per cent of their activity in one year.

Highly concentrated peroxide was of great war-time importance because of its use as a fuel for jet propelled missiles. At first, high concentration peroxide was used merely for the superheated steam and oxygen formed during its decomposition and which was capable of driving turbines. Later development, however, utilized the oxygen with liquid fuel. This type of peroxide-fuel combination was used for jet propulsion purposes for rockets, etc. Torpedoes and submarines fueled with hydrogen peroxide had the advantage of producing no distinguishable line of air bubbles when in motion.

The methods used for the commercial production of hydrogen peroxide for medicinal and industrial use may be divided into two major classifications: (1) the non-electrolytic and (2) the electrolytic.

*Non-electrolytic* hydrogen peroxide is made (1) by the action of sulfuric or phosphoric acid on hydrated barium peroxide, (2) by the action of sulfuric acid upon a solution of sodium peroxide, (3) by reduction and subsequent oxidation of 2-ethyl anthraquinone and (4) by direct synthesis from hydrogen and oxygen influenced either by a high-frequency electric discharge or by a suitable catalyst.

1. Barium peroxide is produced by passing dry air over barium oxide that has been heated to about 600° C. In order that the reaction with sulfuric or phosphoric acid can go to completion, the peroxide is hydrated by a special steam treatment which gives a white, crystalline hydrate of the approximate formula, BaO<sub>2</sub>.8H<sub>2</sub>O. When this is suspended in distilled water contained in a large glass-lined steel tank and dilute sulfuric or phosphoric acid added, hydrogen peroxide is liberated and barium sulfate or normal barium phosphate is precipitated (13) (14). When sulfuric acid is used, the hydrated barium peroxide is sometimes subjected to a preliminary treatment with hydrochloric acid to effect a more complete reaction. The precipitated barium sulfate (*blanc fixe*) is filter-pressed and washed. It is used in the paper industry and as a pigment. The hydrogen peroxide is distilled and adjusted to the desired strength by the addition of distilled water.



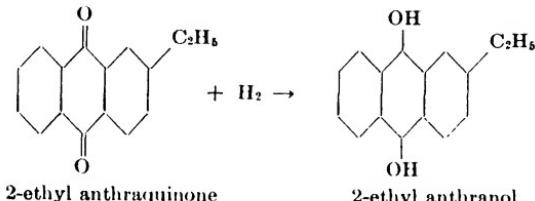
2. Higher concentrations of hydrogen peroxide for industrial use (bleaching) are often made by treating a solution of sodium peroxide with sulfuric acid (15), removing all but about 3 per cent of the mineral matter by adding sodium fluoride and cooling to about -2° C.



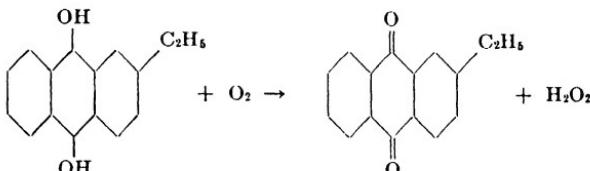
Although hydrogen peroxide by this method is unfit for medicinal use, the impurities present do not preclude its industrial use.

3. Because of shortage of electrical power due to intensive Allied bombing during the war,<sup>1</sup> the reduction of 2-ethyl anthraquinone (16) and the subsequent oxidation (17) of the resultant 2-ethyl anthranol offered an attractive non-electrolytic peroxide synthesis to German chemists.

(16)



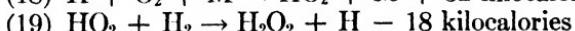
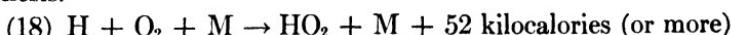
(17)



While actual production of hydrogen peroxide by this method had not had time to expand before the end of the war, the method nevertheless offers a good, non-electrolytic process not requiring an elaborate setup. The chief disadvantage of this method lies in the difficulty of removing all organic material from the peroxide solutions. The presence of this organic material results in a somewhat unstable and dangerously explosive product.

4. The direct synthesis of hydrogen peroxide from hydrogen and oxygen is a desirable method because the product is exceptionally pure and labor costs are at a minimum due to automatic operation. The most important method of direct synthesis is that developed by the Electrochemische Werke (a German firm) in which hydrogen and oxygen are made to combine directly under the influence of a high-frequency electric discharge. The operation is continuous and is said to require very little attention once it has started.

An interesting method for the preparation of H<sub>2</sub>O<sub>2</sub> by direct combination of the elements H<sub>2</sub> and O<sub>2</sub> appeared in a recent patent.<sup>2</sup> The synthesis is dependent upon the activity of catalytic surfaces (particularly tubes with smooth, dense surfaces coated with fused boric acid or metal borates) which cause the union of H<sub>2</sub> and O<sub>2</sub>. Hydrogen and air (approximately 20 per cent O<sub>2</sub>) are passed through the heated (520° C.) reaction tube. The following equations (18) (19) are thought to represent the reactions taking place in this synthesis.



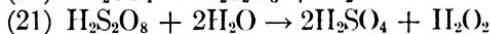
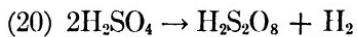
<sup>1</sup> Axis Manufacture of Hydrogen Peroxide, Chem. Ind., **58**, 957, (1946).

<sup>2</sup> U. S. Patent 2,368,640; see also J. Chem. Ed., **22**, 286 (1945).

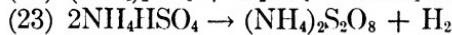
M is any third molecule in the gas phase or surface of the reaction vessel.

*Electrolytic* hydrogen peroxide is prepared (1) by the electrolysis of sulfuric acid to persulfuric acid which is hydrolyzed to yield the product and (2) by the electrolysis of ammonium bisulfate solutions to ammonium persulfate which may be treated in various ways to yield hydrogen peroxide.

1. In this process sulfuric acid is oxidized anodically to persulfuric acid,  $\text{H}_2\text{S}_2\text{O}_8$ , (20) which, in turn, is hydrolyzed to hydrogen peroxide and sulfuric acid (21).

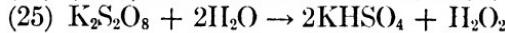


2. A more usual way is to mix ammonium sulfate and sulfuric acid in the proportions to form ammonium bisulfate (22) and electrolyze the cold solution to form ammonium persulfate (23) at the anode.

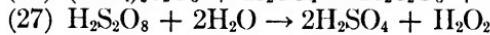
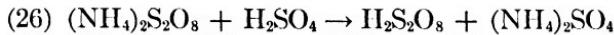


The ammonium persulfate that is formed is usually treated in one of three ways to yield hydrogen peroxide.

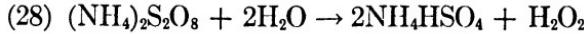
(a) It may be reacted with potassium bisulfate (24) to form relatively insoluble potassium persulfate which can be hydrolyzed by live steam to yield hydrogen peroxide and potassium bisulfate (25), the vapors being condensed and rectified to obtain the hydrogen peroxide.



(b) The ammonium persulfate may be treated with sulfuric acid and distilled at reduced pressures to give a distillate of water and hydrogen peroxide (26) (27).



(c) According to the Kufstein procedure hydrogen peroxide may be distilled directly from the ammonium persulfate solution (28).



All of the foregoing procedures, non-electrolytic and electrolytic, produce a solution of hydrogen peroxide which may be concentrated by distillation under reduced pressure in a suitable apparatus to produce concentrations up to 90 per cent  $\text{H}_2\text{O}_2$ .

**Laboratory Preparation.**—Introduce 3 Gm. of hydrated barium peroxide into an Erlenmeyer flask and add 50 cc. of cold distilled water in divided portions, shaking the flask after each addition. Agitate the mixture frequently for one-half hour. In another flask

dilute 1 cc. of phosphoric acid with 25 cc. of distilled water and cool the mixture in an ice-bath. Now add small portions of the suspension of hydrated barium peroxide to the dilute acid solution, keep the mixture cold in an ice-bath and shake it well after each addition. Allow the precipitate to settle, decant the supernatant liquid by means of a glass syphoning tube and filter the remainder. To the filtrate add diluted sulfuric acid drop by drop as long as any precipitate forms. Mix sufficient starch with the liquid to make it appear milky, shake it well and filter rapidly. Collect the filtrate in a bottle of suitable size and stopper immediately.

NOTE.—Because of difficulties in filtering the large volumes of precipitate formed when an official 3 per cent peroxide is made in small quantities, this method gives a solution approximately one-tenth the strength of the official.

**Pharmaceutical Preparations and Uses.**—1. *Hydrogen Peroxide Solution* (*Liquor Hydrogenii Peroxidi*, *Hydrogen Dioxide Solution*), U. S. P. XIII, is an aqueous solution containing, in each 100 cc., not less than 2.5 Gm. and not more than 3.5 Gm. of  $H_2O_2$ . It is a colorless liquid, odorless or having an odor resembling that of ozone. The solution, when free from impurities, keeps fairly well. A trace of free acid and acetanilid increases its stability by catalytically retarding its decomposition. When exposed to the air at ordinary temperatures or when heated on a water-bath at a temperature not exceeding 60° C., the solution loses chiefly water. In this way the solution may be concentrated so as to contain 50 per cent by volume of hydrogen dioxide. When rapidly heated, it frequently decomposes suddenly. Because of impurities in the reacting substances used in the manufacture of solutions of hydrogen dioxide, the U. S. Pharmacopœia XIII specifies that the official solution be practically free from arsenic, barium and heavy metals. The amount of non-volatile matter is limited to 0.15 Gm. in 100 cc. of the solution; the free acidity in 100 cc. must not exceed an equivalent of 10 cc. of tenth-normal sodium hydroxide solution; and the preservative (usually acetanilid) must not exceed 50 mg. per 100 cc. of solutoin. This solution is used as an antiseptic because of the active liberation of oxygen when it comes in contact with organic material (*e. g.*, pus and blood). The foaming caused by the liberation of  $O_2$  mechanically cleanses wounds by dislodging fixed bacteria, particles of dirt, etc. This mechanical action rather than its chemical antisepsis is its important function, since the period of contact of oxygen with the bacteria is too short to bring about an effective oxidizing action, and  $H_2O_2$  itself is only feebly antiseptic. The 3 per cent solution is also used in treating Vincent's stomatitis, the undiluted solution being used as a mouth wash several times daily. Continued use may cause a condition known as "hairy tongue" (*hypertrophied filiform papillæ*), which disappears on discontinuation of the medication. It is also a chemical antidote for cyanide and phosphorus poisoning through oxidation of the poisonous materials to more or less harmless oxidation products.

2. Stronger solutions of hydrogen peroxide are used as hair bleaches, fabric bleaches, etc. They are particularly desirable because of the harmless nature of the reaction products. Usually a 6 per cent solution (20 volume) is considered adequate as a hair bleach. A small amount of dilute ammonia solution is usually combined with the peroxide for hair application to soften the hair and hasten the bleaching process.

Solutions of hydrogen peroxide are frequently said to be of a certain "volume" strength (*i. e.*, 10 volume, 20 volume, etc.). Ordinary 3 per cent hydrogen peroxide solution is a 10 volume peroxide, 6 per cent peroxide is 20 volume, etc. A common commercial strength is 100 volume or 30 per cent hydrogen peroxide. The volume specification is based on the number of cubic centimeters of oxygen, measured at standard temperature and pressure, liberated by 1 cc. of the peroxide solution when decomposed (2). Thus, if 1 cc. liberates 10 cc. of oxygen it is a 10 volume peroxide, etc.

## CHAPTER IV

### NITROGEN, NITROUS OXIDE, AND AMMONIA

#### NITROGEN

Symbol, N. Valence, 3 and 5. Atomic Weight, 14.008.  
Atomic Number, 7

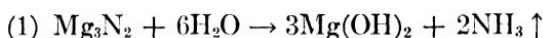
**History.**—In 1772, Dr. D. Rutherford of Edinburgh, observed that when oxygen was removed from air there remained a gas which was incapable of supporting either combustion or respiration. In the published results of his work, he designated this gas as "mephitic air." Scheele was the first to understand the true nature of the principal gases composing the atmosphere. He showed that one gas (oxygen) supported combustion and respiration and that the other (nitrogen) did not. Lavoisier proved conclusively the correctness of Scheele's findings, and he named the inert gas *azote* from the Greek meaning "without life." Because this element was found to be a constituent of saltpeter, Chaptal proposed the name *nitrogen*, from the Greek, *νιτρον*, niter, and *γενῶ*, I produce, and it was generally accepted. In 1894, Rayleigh and Ramsay showed that atmospheric nitrogen was in reality an admixture of nitrogen and slightly over 1 per cent of inert gases.

**Occurrence.**—Nitrogen constitutes approximately 79 per cent by volume of the atmosphere. Free nitrogen is found in some natural waters. Spectroscopic observations have shown it to be present in certain nebulae and probably in the sun. In combination with sodium and oxygen, it occurs in Nature in enormous quantities as Chile saltpeter. When united with hydrogen, it forms ammonia (free or combined) and, in organic combination as protein, amino-acids, etc., it is an integral part of animal and vegetable tissues and liquids. It is invariably present in soil, wherein nitrogen compounds are formed by the action of nitrifying bacteria.

**Physical Properties.**—Nitrogen is a colorless, tasteless and odorless gas. Its density is 0.9682 (air = 1). One liter of nitrogen at 0° C. and 760 mm. weighs 1.2506 Gm. Nitrogen can be liquefied; the critical temperature being -147.13° C. and the critical pressure 33.49 atmospheres. It forms a colorless liquid, boiling at -195.8° C. and a white solid melting at -209.8° C. Under standard conditions (0° C. at 760 mm.), 2.3 volumes of nitrogen dissolve in 100 volumes of water.

**Chemical Properties.**—Nitrogen is a very inert gas. Like hydrogen, it may be activated by high voltage discharges at low pressure or by subjecting the gas at normal pressure to a silent electrical discharge. It will neither burn nor support the combustion of ordinary combustibles. At high temperatures, it combines directly

with Li, B, Si, Ba, Ca, Sr and Mg to form nitrides. Thus, when magnesium ribbon is burned in air, the white powder that is formed is composed of large quantities of magnesium oxide ( $MgO$ ) and smaller quantities of magnesium nitride ( $Mg_3N_2$ ). The latter compound may be detected by moistening the ash with water and testing the evolved gas with moistened litmus paper (red). The paper is turned blue by the ammonia produced by the hydrolysis of the nitride (1).



When the rare earth metals are mixed with magnesium and heated in a current of nitrogen, nitrides are produced.

Nitrogen forms six oxides: Nitrous oxide,  $N_2O$  (*q. v.*); nitric oxide,  $NO$ ; nitrogen trioxide,  $N_2O_3$ ; nitrogen dioxide,  $NO_2$ ; nitrogen tetroxide,  $N_2O_4$ ; and nitrogen pentoxide,  $N_2O_5$ . It slowly and difficultly combines with hydrogen to form ammonia,  $NH_3$ , hydrazine,  $N_2H_4$ , and hydrazoic acid,  $N_3H$ . Chlorine unites with it to form a very volatile, oily, yellow substance ( $N : Cl_3$ ), which has a very pungent smell, powerful lachrymatory properties, and is a most dangerous explosive. The corresponding iodine compound has been prepared.

**Commercial Manufacture.**—Nitrogen may be obtained experimentally by (1) removing the oxygen from the atmosphere or (2) by decomposing compounds in which it occurs.

The first may be accomplished by:

1. Burning phosphorus in a confined volume of air. The phosphorus combines with the oxygen of the air to form phosphorus pentoxide,  $P_2O_5$ . The gas remaining in the container is nearly pure nitrogen.

2. The action of an alkaline solution of pyrogallol on air. An alkaline solution of pyrogallol energetically absorbs oxygen from the air, turns brown, and finally decomposes into carbon dioxide, acetic acid, and brown substances. Nitrogen is unaffected by the pyrogallol solution.

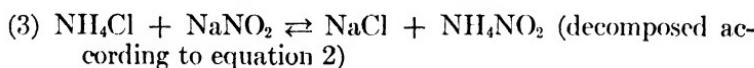
3. Passing air over red-hot copper filings. Copper at red heat combines with the oxygen of the air to form copper oxide, whereas the nitrogen is unaffected and passes on into a reservoir.

It may be obtained from some of its compounds in the following ways:

1. By heating a slightly acidulated solution of ammonium nitrite (2).



2. By heating a mixture composed of concentrated solutions of sodium nitrite and ammonium chloride (3).



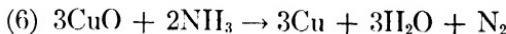
3. By the action of chlorine or bromine upon ammonia or ammonium hydroxide (4).



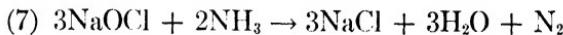
4. By heating ammonium nitrate with ammonium chloride and passing the evolved gases through a solution of sodium hydroxide to absorb the chlorine (5).



5. By passing ammonia gas over heated copper oxide (6).



6. By oxidizing ammonia with a hypochlorite (7).

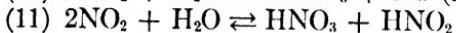
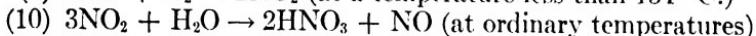
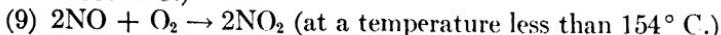
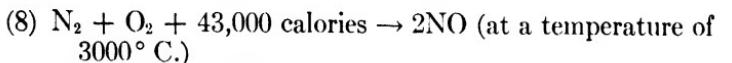


For the production of quantities sufficient for industrial use (manufacture of cyanamid, etc.) it is made by (1) fractional distillation of liquid air; (2) the fractional separation by liquefaction of producer gas which contains about 67 per cent of nitrogen; (3) by catalytically oxidizing the CO in producer gas to CO<sub>2</sub>; (4) by decomposing ammonia into H<sub>2</sub> and N<sub>2</sub> by passage over heated iron and then liquefying the nitrogen.

**Nitrogen Fixation.**—Nitrogen is a necessity for the development of living plants. Plants do not have the power of fixing atmospheric nitrogen as they do oxygen and, therefore, must obtain it from nitrogenous compounds formed in the soil mainly by the action of nitrifying bacteria. Because these compounds are essential to plant life, it is necessary to replace them as they are extracted from the soil; hence the use of nitrogenous manures or artificial fertilizers containing soluble nitrates. The enormous demands made upon the niter deposits have brought about the realization that eventually these natural sources of nitrogen will be used up. The attention of chemists has turned to the development of processes for the fixation of atmospheric nitrogen in order to establish an independence of the rapidly diminishing natural sources of nitrates and also for economic reasons. Combination of nitrogen, obtained directly or indirectly from the air, can be effected by forming (1) oxides of nitrogen and nitric acid, (2) ammonia, (3) decomposable nitrides, (4) cyanides, (5) cyanamides, and (6) urea.

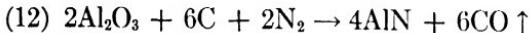
1. *Birkeland-Eyde Process.*—K. Birkeland and S. Eyde devised a process which has been worked on a large scale at Notodden and elsewhere in Norway. An electric arc is produced in a specially constructed furnace by passing an alternating current of about 5000 volts equatorially between the poles of an electromagnet, thereby forming what is practically a disk of flame 6½ feet in diameter and having a temperature of about 3000° C. (5432° F.). Air is blown through the flame in such a way that all of it comes in contact with the heated area, wherein the oxygen and nitrogen combine to

form nitric oxide (NO) (8). The air (containing about 2 per cent of NO) coming from the furnace is rapidly cooled in boilers and aluminum-tube coolers until it reaches ordinary atmospheric temperature. Then it is passed into large open towers constructed of quartz slabs, where the nitric oxide formed in the arc is oxidized to  $\text{NO}_2$  (9) which polymerizes to  $\text{N}_2\text{O}_4$ . The nitrogen tetroxide is led into a series of absorption towers where it meets a descending current of water or dilute nitric acid and is changed into nitric acid (10). The final solution contains between 30 and 35 per cent of  $\text{HNO}_3$ . The unabsorbed gases, weak in oxides of nitrogen, are usually passed into an additional series of iron absorption towers. Here they meet a counter current of soda ( $\text{Na}_2\text{CO}_3$ ) solution with which they form sodium nitrate and some sodium nitrite (11). These compounds are recovered as such. It is also a common practice to pass the weak gases into milk of lime, thus forming basic calcium nitrate, which may be used as a fertilizer. The reactions taking place may be represented as follows:

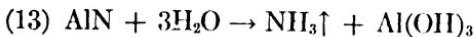


In the Badische Analin und Soda Fabrik method (Schönherr Process), the arc, which is said to be over 30 feet in length, is formed in a long tube and a stream of air is injected spirally, thus exposing every part of it to the electrical discharge.

2. *The Serpek Process.*—In this process bauxite (impure aluminum oxide) is mixed with coke and heated to a temperature of about  $1800^\circ$  C. in an electrical furnace through which nitrogen, obtained in one of the usual ways (p. 65) is being passed (12).



The crystalline aluminum nitride so formed is treated with steam under pressure. Ammonia and a pure form of aluminum hydroxide is produced (13).



The hydroxide is then ignited to form a white amorphous powder of the oxide (14).



The ammonia may be absorbed in water, oxidized to nitric acid, or used in liquefied form for refrigerating purposes.

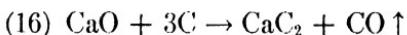
3. *The Bucher Process.*—In 1917, Prof. J. C. Bucher of Brown University, succeeded in making sodium cyanide and a ferrocyanide by passing producer gas through a heated tube filled with briquets made of soda ash, iron and coke. At the high temperature, and in

the presence of the catalyst (iron), the nitrogen contained in the producer gas reacts to form sodium cyanide and the carbon is burned off as carbon monoxide (15).



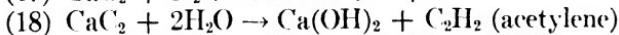
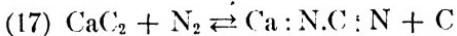
Aside from the many industrial uses of sodium cyanide, it may be converted into ammonia by hydrolysis.

4. *The Frank and Caro Cyanamide Process.*—This process depends upon the fixation of nitrogen as calcium cyanamide by means of calcium carbide. First, calcium carbide is made in any one of several types of electric furnaces. In the Horry type, which is a continuously operating furnace, finely powdered lime is mixed with powdered coke and charged into a drum equipped with carbon electrodes. The drum makes one complete revolution in about two days. The resistance of the material to the electric current raises the temperature of the physical mixture to the point where the following chemical reaction takes place (16).



Liquid carbide (M. P. about  $2000^{\circ}$  C.) collects at the base, cools, and solidifies. In about a day it has reached the opposite side of the drum and can be removed without interrupting the operation.

The calcium carbide thus produced is finely ground in tube mills under an atmosphere free from moisture and oxygen, and placed in large iron drums. The charge is heated electrically, a centrally located carbon rod serving as one electrode and the container as the other. The nitrogen is turned on and is absorbed so rapidly by the hot carbide that the evolved heat is sufficient to keep the mass at the reaction temperature (about  $1100^{\circ}$  C.) and, therefore, the carbon rod is withdrawn (17). The resulting dark gray mass is composed of calcium cyanamide (about 60 per cent) and carbon and is known as *nitro-lime*. This is sprayed with only enough cold water to decompose any excess calcium carbide (18), then mixed with a solution of sodium hydroxide and treated with steam in an autoclave or pressure digester under a pressure of from 3 to 4 atmospheres (19).

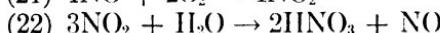
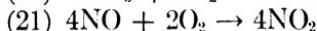
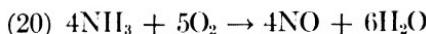


The evolved ammonia is absorbed by water or it is converted into ammonium nitrate. The sludge is freed of dissolved ammonia by blowing steam through it.

5. *The Haber Process.*—The synthesis of ammonia from its constituent elements is one of the most important methods of nitrogen fixation (see p. 72).

If it is desired to use the nitrogen, fixed as ammonia, for the production of nitrates, it is necessary to first convert the ammonia

into nitric acid. This is accomplished by means of the *Ostwald Process*, whereby ammonia is mixed with air (21 per cent of oxygen), the mixture heated and rapidly passed through a fine wire gauze of activated platinum raised to a glowing heat. Better than 95 per cent of the ammonia is oxidized to NO, and then to NO<sub>2</sub> (20, 21, 22), which is absorbed by water to form nitric acid.



The nitric acid so formed may be used as such or converted into sodium nitrate, calcium nitrate, etc.

**Uses.**—Elementary nitrogen is used principally in connection with nitrogen fixation. The Haber process for ammonia production uses the largest amount. Considerable quantities of nitrogen are also used in the cyanamide process.

Inorganic nitrogen consumption in the United States has expanded considerably in recent years, and it is difficult to conceive of a possible shortage in the future for agricultural needs. The following table supplies an idea of our growing nitrogen needs:

1940	1941	.	.	405,000 short tons
1941	1942	.	.	350,000 short tons
1942	1943	.	.	434,000 short tons
1943	1944	.	.	605,000 short tons
1944	1945	.	.	675,000 short tons
1945	1946	.	.	699,000 short tons

Nitrogen is used in smaller quantities when a chemical process requires an inert atmosphere as in some organic chemistry reactions and in the assay for carbon monoxide in oxygen. Mercury thermometers that are intended for use at elevated temperatures  $>200^\circ$  have the space above the mercury column filled with nitrogen to decrease the evaporation of the mercury and to prevent its oxidation. Electric light globes filled with nitrogen are now in general use, thus giving longer life by reducing the volatilization of the tungsten filaments. Cod-liver oil and castor oil are often packaged with a nitrogen atmosphere above the oil to retard oxidation (and consequent rancidity) during storage.

## NITROUS OXIDE

### Nitrous Oxide, U. S. P. XIII

Formula, N<sub>2</sub>O. Molecular Weight, 44.02

**History.**—Nitrogen monoxide or nitrous oxide was first made in 1772 by J. Priestley. He obtained it by the action of nitric oxide (NO) upon moist iron filings. While studying the physical and chemical properties of this gas, he observed that ignited substances burned in it with greater luminosity than in the atmosphere. In 1800 Sir H. Davy, who determined its composition, observed that

the gas produced exhilarating effects when inhaled, hence its common name "laughing gas."

**Physical Properties.**—Nitrous oxide is a colorless gas, having a slight, characteristic odor. Its aqueous solutions have a somewhat sweetish taste. Its specific gravity is 1.530 (air = 1). One liter of the gas at 0° C. and one atmosphere pressure weighs 1.9778 Gm. and it is readily soluble in water at low temperatures. Under normal pressure 100 volumes of water dissolve about 180 volumes of the gas at 0° C., in about 67 volumes at 20° C., and in about 59.4 volumes at 25° C. One volume of nitrous oxide dissolves in about 1.5 volumes of water under normal pressure at 20° C. It is about three times more soluble in alcohol than in water, and readily dissolves in ether and in oils. The gas may be liquefied to a thin, mobile, colorless liquid boiling at -89.5° C. When it is further cooled, white crystals melting at -102.4° C. separate out.

**Chemical Properties.**—Nitrogen monoxide is not inflammable but it supports the combustion of many substances almost as well as oxygen. It supports the combustion of a glowing splinter of wood and phosphorus and sulfur burn in it. Metals do not rust in nitrous oxide. The hemoglobin of the blood is unable to use it as a source of oxygen.

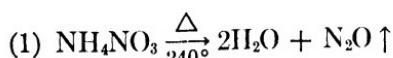
**Official Tests for Purity.**—The U. S. Pharmacopœia requires that carbon dioxide, halogens, acids or alkalies, reducing substances, and oxidizing substances be either absent or limited in amount.

*Note.—Cylinders containing Nitrous Oxide must be kept at a temperature of 25°, ±2°, for at least six hours before the Nitrous Oxide is withdrawn for the following determinations. Gas volumes for the following tests and assays are to be corrected to a pressure of 760 mm. and a temperature of 25°.*

For an explanation of the tests for purity see the discussion under Carbon Dioxide.

Nitrous Oxide contains not less than 95 per cent by volume of N<sub>2</sub>O and is supplied in tight metal cylinders.

**Commercial Manufacture.**—Ammonium nitrate, which is absolutely free from chlorides and other impurities, is gradually heated to about 200° C. in aluminum retorts. At this temperature decomposition into nitrous oxide and water begins (1).



The temperature is then slowly raised to 240° C. This temperature should not be exceeded lest the nitrous oxide becomes contaminated with nitrogen, ammonia, and other oxides of nitrogen. The gas is cooled in a condenser, washed with sodium dichromate solution to remove nitric oxide, with a solution of sodium hydroxide to take out the nitric acid, and lastly with water. It is then compressed in steel cylinders under a pressure of about 100 atmospheres.

**Pharmaceutical Preparation and Uses.**—1. *Nitrous Oxide* (Oxidum Nitrosum, Nitrogen Monoxide), U. S. P. XIII.—Nitrous oxide con-

tains not less than 95 per cent by volume of  $\text{N}_2\text{O}$ . Nitrous oxide is used to produce conditions of analgesia and anesthesia. In order to prevent shock, the nitrous oxide is usually mixed in a common reservoir with approximately 4 per cent of oxygen and administered to the patient for one minute. The oxygen is then cut off and pure nitrous oxide given for forty seconds additional, when complete anesthesia usually results.

### AMMONIA

Formula,  $\text{NH}_3$ . Molecular Weight, 17.03

**History.**—An aqueous solution of ammonia was prepared during Geber's time (eighth century) by destructively distilling the hoofs and horns of animals and absorbing the gas in water. The solution was called "spirit of hartshorn." In 1756 Black differentiated between ammonia and ammonium carbonate. Priestley was the first to obtain almost pure ammonia and he called it "alkaline air." Berthollet determined its composition in 1803.

**Physical Properties.**—Ammonia is a colorless gas having a strong, pungent, characteristic odor. It is about one-half as heavy as air, having a specific gravity of 0.589 (air = 1). One liter of ammonia weighs 0.7710 Gm. The gas may be liquefied either by subjecting it to intense cold ( $-60^\circ \text{ C}.$ ) or by cooling it to about  $10^\circ \text{ C}.$  and increasing the pressure to 6.5 or 7 atmospheres. Liquid ammonia boils at  $-33.35^\circ \text{ C}.$  and the white crystals of solid ammonia melt at  $-77.7^\circ \text{ C}.$  Liquid ammonia is a good solvent and ionizing medium.

One cubic centimeter of water at  $0^\circ \text{ C}.$  dissolves 1298.9 volumes of ammonia, and at  $15^\circ \text{ C}.$  1 cc. of water dissolves 727 volumes of the gas. Its solutions are lighter than water. It is also soluble in alcohol and ether. All of the gas may be expelled from its solutions by boiling. Ammonia exists in aqueous solution mainly in the form  $\text{NH}_3$ , only a small amount reacting with water to form  $\text{NH}_4\text{OH}$ .



For all practical purposes, however, ammonia water may be considered as containing  $\text{NH}_4\text{OH}$ .

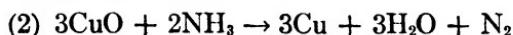
**Chemical Properties.**—At low temperatures ammonia is stable. At red heat and by the action of an electric spark, it is completely decomposed into hydrogen and nitrogen. The reaction is reversible (1).



The gas does not burn in air, but in oxygen it burns with a yellowish flame forming nitrogen, nitric oxide and ammonium nitrite.

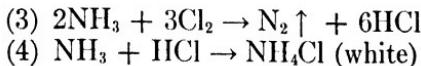
Heated ammonia is an active reducing agent.

Heated oxides of many metals are reduced when ammonia is passed over them (2).

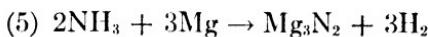


However, when a mixture of ammonia and air is heated in the presence of a catalyst (platinum), the ammonia is oxidized to water and oxides of nitrogen which combine to form nitric acid.

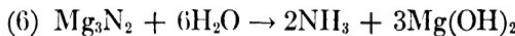
When a current of either chlorine or bromine vapor is passed into a flask containing ammonia, the halogen catches fire and free nitrogen and ammonium chloride or ammonium bromide are formed (3 and 4).



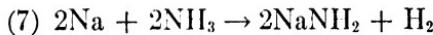
When lithium, calcium, magnesium or boron are heated in a stream of ammonia gas, hydrogen is evolved and the respective nitride formed (5).



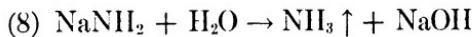
These nitrides are solids and are easily hydrolyzed by water to ammonia (6).



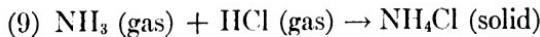
Sodium and potassium replace only part of the hydrogen of ammonia. The resulting compounds are known as amides (7).



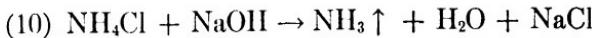
Sodamide, like the nitrides, yields ammonia upon hydrolysis (8).



Ammonia combines with acids to form ammonium salts (*q. v.*), (9).

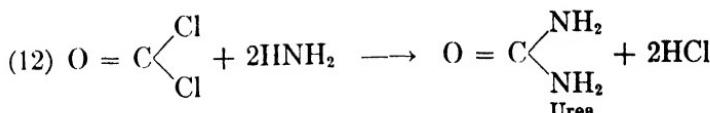
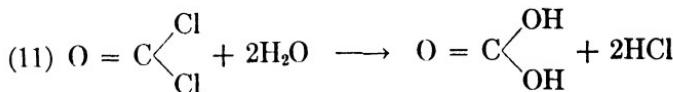


The action of strong bases will liberate ammonia from its compounds (10).

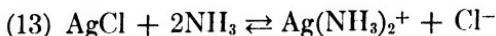


Ammonia of crystallization does occur with some compounds such as  $\text{CaCl}_2 \cdot 8\text{NH}_3$ .

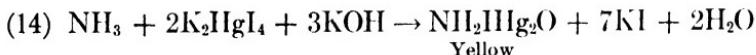
Ammonia reacts with active chemical groups in a way similar to that of water. Phosgene with water results in the formation of carbonic acid and hydrogen chloride. Such a reaction is known as *hydrolysis* (11). An analogous reaction with ammonia is called *ammonolysis* (12).



Ammonia readily forms soluble complex ions with certain metals namely Ag, Cu, Zn, Cd, Ni, and Co. A common example is the formation of the complex silver-ammonia ion when AgCl (insoluble) is treated with ammonia in excess (13).



**Official Test for Identity.**—When ammonia ( $\text{NH}_3$ ) is present in colorless solutions it may be detected with Nessler's Reagent. When 2 cc. of alkaline mercuric potassium iodide T.S. are added to an aqueous solution containing ammonia a deep yellow color is produced (14).



**Commercial Manufacture.**—Ammonia is produced at the present time almost exclusively by the Haber Process or some modification of it. The wash-waters of the gases obtained by the destructive distillation of coal (production of coke and illuminating gas) are also a source of ammonia. Ammonia, as a constituent of *crude* illuminating gas combines in part with various other impurities to form salts, *e. g.*, the carbonates,  $\text{NH}_4\text{HCO}_3$ ,  $(\text{NH}_4)_2\text{CO}_3$ , etc.; sulfides,  $\text{NH}_4\text{HS}$ ,  $(\text{NH}_4)_2\text{S}$ , etc.; cyanide,  $\text{NH}_4\text{CN}$ ; chloride,  $\text{NH}_4\text{Cl}$ ; and sulfate,  $(\text{NH}_4)_2\text{SO}_4$ . The water condensed in the *hydraulic main* contains a considerable quantity of so-called fixed ammonium compounds (ammonium chloride, sulfate, etc.) whereas the water condensed in the cooler parts of the condensing system contains a high "volatile-ammonia" content. In most gas works, the mixture composed of gas-condensate and scrubber-water will have an ammonia content of about 3 per cent by weight. This *ammoniacal gas liquor* is first concentrated to 16 per cent ammonia and shipped in tank cars to ammonia refineries.

**The Haber Process.**—The synthesis of ammonia from its constituent elements has been a commercial success for a number of years. When nitrogen and hydrogen are mixed in volume proportions of 1 to 3 and the mixture under high pressure (200 atmospheres) passed through a catalyst heated to about  $550^\circ \text{C}$ ., they unite to form ammonia. The nitrogen for this process is obtained from producer gas, which is composed essentially of two volumes of nitrogen and one volume of carbon monoxide; and water gas, consisting of about equal volumes of hydrogen and carbon monoxide, is the usual source of the hydrogen. The mixture of water gas and producer gas is mixed with steam and passed through a hot catalyst. Here the carbon monoxide is oxidized to carbon dioxide and additional hydrogen is produced. At this point the volumes are adjusted so as to give a ratio of 1 of nitrogen and 3 of hydrogen, and the mixed gases, under a pressure of about 50 atmospheres, are scrubbed with water and finally with a solution of caustic soda to remove any remaining carbon dioxide. The pressure is then stepped up to 200 atmospheres, the gases scrubbed with ammoniacal

copper formate to remove carbon monoxide and passed on to the catalyzing elements. The catalyst is said to be a mixture of metallic oxides, *e. g.*,  $\text{Fe}_3\text{O}_4$ ,  $\text{Fe}_2\text{O}_3$ , and  $\text{Al}_2\text{O}_3$ , containing about 1 per cent of  $\text{K}_2\text{O}$ . The gases leaving the catalyzing element contain about 8 per cent by volume of ammonia, which is cooled and absorbed in water. The uncombined nitrogen and hydrogen are dried and again passed through the apparatus. The reaction taking place may be represented as follows (15):



This reaction is reversible and exothermal. At low temperatures no union occurs, whereas at  $700^\circ \text{ C}$ . any ammonia produced is entirely decomposed. Therefore, the combination must take place under pressure and at approximately  $500^\circ \text{ C}$ ., at which temperature about 8 per cent of the gases (hydrogen and nitrogen) combine in the presence of a catalyst to form ammonia. The combination is accompanied always by a decrease from 4 to 2 volumes of gas. The ammonia may be recovered easily from the ammonia water in continuously operating stills and then, if desired, it may be liquefied. In this physical state it may be used for refrigeration or other purposes. Modifications of this process are: the General Chemical which employs about 100 atmospheres; the Casale uses about 700 atmospheres; and the Claude about 1000 atmospheres. At the higher pressures the ammonia yields are considerably higher and it can be removed directly as liquid ammonia.

**Pharmaceutical Preparations and Uses.**—1. *Strong Ammonia Solution* (Liquor Ammoniae Fortis, Stronger Ammonia Water, Stronger Ammonium Hydroxide Solution), U. S. P. XIII.—Strong Ammonia Solution is an aqueous solution of ammonia ( $\text{NH}_3$ ) containing not less than 27 per cent and not more than 29 per cent of  $\text{NH}_3$ . This solution deteriorates rapidly in open containers.

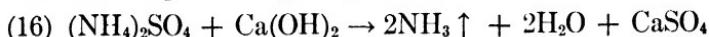
*Caution.*—*Great care should be used in handling Strong Ammonia Solution because of the caustic and irritating properties of its vapors. Before the container is opened it should be well cooled and the closure covered with a towel before removal. Strong Ammonia Solution must never be tasted nor its vapors inhaled.*

Strong Ammonia Solution is a colorless, transparent liquid, having an exceedingly pungent, characteristic odor, and a very caustic and alkaline taste. It is strongly alkaline to litmus and has a specific gravity of 0.90.

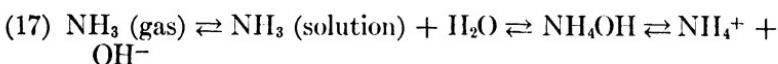
**Commercial Manufacture.**—Strong ammonia solution is prepared by passing ammonia gas into cooled water until the water is saturated with ammonia ( $\text{NH}_3$ ).

**Laboratory Preparation of Diluted Ammonia Solution.**—Place 72.6 Gm. of ammonium sulfate in a flask provided with safety tube and outlet. In another dish slake 31 Gm. of lime and add sufficient water to make a milk of lime. Add the milk of lime to the ammonium sulfate and immediately connect the outlet with a tube, one end of which extends to the bottom of a cylinder containing 200 cc. of cold,

distilled water. Gently heat the flask containing the reaction mixture, so as to obtain a steady and not too rapid evolution of ammonia (16). The absorption cylinder may be kept cool by standing it in a jar filled with cold water. The entire apparatus should be erected under a ventilating hood. When the evolution of ammonia has ceased, determine the degree Baumé of the product, and from this calculate the per cent by weight of ammonia.



At or below the temperature  $-79.3^{\circ}$  C., ammonia chemically combines with water to form a white, solid ammonium hydroxide. Ammonium hydroxide (solid) dissociates at temperatures above that previously mentioned, hence it is available only in the form of its solution. In a normal solution (about 1.7 per cent) only 0.4 per cent of ammonium hydroxide is dissociated into ammonium ion ( $\text{NH}_4^+$ ) and hydroxide ion ( $\text{OH}^-$ ). The remainder of the ammonia is present in the solution as free ammonia, as undissociated ammonium hydroxide, or as traces of ammonium oxide ( $\text{NH}_4\text{O}$ ). When hydronium ions (from HCl for example) are introduced into the solution, the equilibrium is disturbed by the union of hydroxide ions with hydronium ions to produce water, and the ammonium ions and chloride ions unite to form ammonium chloride. As rapidly as water is formed by the hydroxide ions uniting with hydronium ions, more ammonium hydroxide dissociates into its cation and anion, and concurrently more ammonia combines with water to form undissociated ammonium hydroxide. This effort to reestablish an ionic equilibrium continues until the reaction is complete (17) and (18).



The weak basic property of an aqueous solution of ammonium hydroxide is due to the presence of relatively few  $\text{OH}^-$ , produced by the slight dissociation of ammonium hydroxide into  $\text{NH}_4^+$  and  $\text{OH}^-$ .

The quantity of  $\text{NH}_4\text{OH}$  is very small in relation to the quantity of ammonia ( $\text{NH}_3$ ) in an aqueous solution of ammonia. In a 0.1 M solution of ammonia ( $\text{NH}_3$ ) the molar concentration of  $\text{OH}^-$  ions is approximately  $\frac{1}{100}$  that of the concentration of ammonia ( $\text{NH}_3$ ).

On account of its ability to unite directly with acids, an aqueous solution of ammonia is used in the manufacture of ammonium salts (*q. v.*). It is also used in the manufacture of sodium bicarbonate (*q. v.*), nitric acid (*q. v.*), etc.

*2. Diluted Ammonia Solution* (*Liquor Ammoniæ Dilutus, Ammonia Water, Diluted Ammonium Hydroxide Solution*), U. S. P. XIII.—Diluted Ammonia Solution is a solution of  $\text{NH}_3$  containing in each 100 cc. not less than 9 Gm. and not more than 10 Gm. of  $\text{NH}_3$ . This solution deteriorates rapidly in open containers.

It is a colorless, transparent liquid, having a very pungent, characteristic odor. It turns red litmus paper blue and has a

specific gravity of 0.96. Gaseous hydrogen chloride near the mouth of a bottle containing diluted ammonia solution produces dense white clouds of ammonium chloride.

"Spirit of Hartshorn" (10 per cent ammonia in water) was originally prepared by destructively distilling the horns of small deer and passing the gases ( $\text{NH}_3$ ) into water.

**Commercial Manufacture.**—Diluted ammonia solution may be prepared by the method used for strong ammonia solution or by diluting the strong ammonia solution according to the directions of the U. S. P. XIII. Sufficient distilled water is added to 398 cc. of strong ammonia solution to make 1000 cc.

3. *Aromatic Ammonia Spirit* (*Spiritus Ammoniae Aromaticus*), U. S. P. XIII.—(See p. 269.)

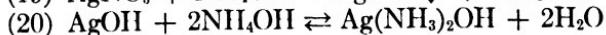
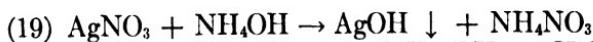
4. *Ammoniated Guaiac Tincture* (*Tinctura Guaiaci Ammoniata*), N. F. VIII.—Aromatic Ammonia Spirit is used as a menstruum. The resins present in guaiac are acidic in nature and form soluble and stable compounds with the alkaline ammonia. Average dose—2 cc. (approximately 30 minims).

5. *Ammonia Liniment* (*Linimentum Ammoniæ*, *Volatile Liniment*, *Hartshorn Liniment*), N. F. VIII.—Oleic acid (10 cc.) is mixed with sesame oil (740 cc.) and when diluted ammonia solution (250 cc.) is added ammonium oleate is formed. The soap thus formed acts as an emulsifying agent and by agitation a uniform mixture is obtained. There is some saponification of the sesame oil to glycerin and ammonium soaps but this is not complete.

6. *Ammonium Valerate Elixir* (*Elixir Ammonii Valeratis*, *Ammonium Valeranate Elixir*), N. F. VIII.—Acid ammonium valerate (35 Gm.) contains about 65 per cent valeric acid which is neutralized with diluted ammonia solution in preparing the elixir. Average dose—4 cc. (approximately 1 fluidrachm).

7. *Ammoniated Valerian Tincture* (*Tinctura Valerianæ Ammoniata*), N. F. VIII.—Valerian contains organic acids, chiefly valeric acid and resin. The presence of alkaline ammonia in the aromatic ammonia spirit used as a menstruum forms soluble and stable compounds with the acids and resin. It is used for its psychological effect. Average dose—2 cc. (approximately 30 minims).

8. *Ammoniacal Silver Nitrate Solution* (*Liquor Argenti Nitratis Ammoniacalis*; *Ammoniacal Silver Nitrate*, *Howe*), N. F. VIII.—Strong ammonia solution is added to a solution of silver nitrate until all except the last traces of the black precipitate that forms (19) has redissolved (20).



This solution is unstable when exposed to light and air. It must be stored in small, well-filled, glass-stoppered, light-resistant containers. Upon opening, the reversible reaction (20) takes place slowly. It is used primarily in dental practice.

9. *Anisated Ammonia Spirit* (*Spiritus Ammoniae Anisatus, Liquor Ammoniae Anisatus*), N. F. VIII.—This is a mixture of the three components, anethole, diluted ammonia solution and alcohol. Its use is similar to that of aromatic ammonia spirit. Average dose—1 cc. (approximately 16 minims).

10. *Bismuth Magma* (*Magma Bismuthi, Milk of Bismuth, Bismuth Cream*), N. F. VIII.—The diluted ammonia solution is used to convert the official ammonium carbonate to normal carbonate (21)



Bismuth hydroxide is also precipitated by the presence of the ammonia solution (22) (see p. 548).



11. *Carmine Solution* (*Liquor Carminii*), N. F. VIII.—Diluted ammonia solution is used to solubilize the carmine (perhaps by salt formation) and to produce a strong deep red solution. This solution is incompatible with liquids having an acid reaction since the carmine may be precipitated and the color destroyed.

12. *Iodides Tincture* (*Tinctura Iodidorum*), N. F. VIII.—This preparation is discussed under iodine (see p. 96).

13. *Solid Petroxolin* (*Petroxolinum Spissum, Petrolatum Saponatum Spissum, Solid Petrox*), N. F. VIII.—The strong ammonia solution (60 cc.) reacts with the oleic acid (320 Gm.) to form ammonium oleate (23).



Yellow wax is used to make a solid product. Balsam of peru is readily incorporated into solid petrox, producing no granulation which may occur with other bases due to the separation of resinous material.

14. *Senega Fluidextract* (*Fluidextractum Senega, Fluidextract of Seneca—snakeroot*), N. F. VIII.—Due to the presence of pectic acids, before adjusting to the final volume of the fluidextract, cautiously add diluted ammonia solution until the product is alkaline to litmus paper and has a slight odor of ammonia. Average dose—1 cc. (approximately 15 minims).

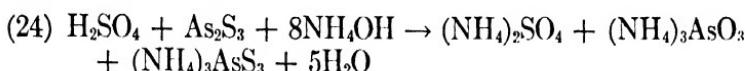
15. *Senega Syrup* (*Syrupus Senegae*), N. F. VIII.—Senega fluid-extract contains pectic acids that are neutralized with diluted ammonia solution before the fluidextract is mixed with syrup. This prevents gelatinization of the finished preparation. Average dose—4 cc. (approximately 1 fluidrachm).

16. *Solid Soap Liniment* (*Linimentum Saponis Spissum, Camphorated Soap Liniment, Solid Opodeldoc*), N. F. VIII.—Diluted ammonia solution is present for its counterirritant properties. The chemistry of this liniment is on page 172.

17. *Soda and Mint Solution* (*Liquor Soda et Menthae, Mistura Soda et Menthae, Soda Mint*), N. F. VIII.—Ammonia is present

as ammonium carbonate, ammonium hydroxide and ammonia due to the aromatic ammonia spirit used. The preparation may be used as a mild gastric antacid. Average dose—8 cc. (approximately 2 fluidrachms).

18. *Washed Sulfur* (Sulfur Lotum), N. F. VIII.—In the preparation of washed sulfur, the sublimed sulfur is macerated for three days in diluted ammonia solution in order to remove any sulfuric acid and arsenic sulfide as ammonium sulfate, arsenite and sulfarsenite (24). (See p. 563.)



**Uses of Ammonia.**—Liquid ammonia is used for refrigeration and for the manufacture of artificial ice. When 1 Gm. of liquefied ammonia evaporates at  $-33.4^{\circ}\text{ C.}$ , it absorbs 330 calories of heat. In order to freeze 1 Gm. of water at  $0^{\circ}\text{ C.}$ , 79 calories of heat must be removed. Therefore, the heat absorbed in the evaporation of 1 Gm. of liquid ammonia, when taken from water is sufficient to convert about 4 Gm. of water at  $0^{\circ}\text{ C.}$  into ice at the same temperature. The practical application of these principles is in the manufacture of "artificial" ice and for refrigeration purposes.

*Household ammonia* is a 10 per cent aqueous solution of  $\text{NH}_3$ . It is used for cleaning and washing, both because of its water softening and saponifying properties. Large quantities of ammonia are used in the production of fertilizers, nitric acid and ammonium salts. The decomposition of ammonia into a mixture of 75 per cent hydrogen and 25 per cent nitrogen by volume is now easily carried out by means of a catalyst. The hydrogen may be conveniently used in oxyhydrogen torches. Liquid ammonia provides a convenient way in which to transport hydrogen—this because hydrogen is difficult to liquefy and therefore must be stored in a gaseous state in steel cylinders.

## CHAPTER V

### THE HALOGEN FAMILY. FLUORINE AND FLUORINE COMPOUNDS

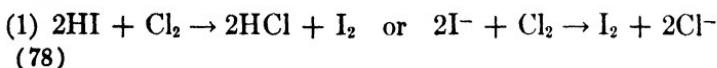
**Introduction.**—Berzelius suggested the word "halogen," which is derived from two Greek words, *ἄλς* (sea salt), and *γεννᾶν* (to produce), and consequently means "the producer of sea salt." The term is applied to four elements—fluorine, chlorine, bromine and iodine, because the sodium salts of their respective hydro-acids are very similar to ordinary sea salt. These four elements and their compounds show a great resemblance to one another in general chemical properties. The physical properties of the elements exhibit a gradual transition. Thus, as the atomic weight increases, the physical state changes from that of a gas (F, 19; Cl, 35.457) to that of a liquid (Br, 79.916) and then to that of a solid (I, 126.92); the melting- and boiling-points rise; the colors deepen; the specific gravities increase; whereas the volatilities and solubilities of these elements decrease in the same order.

All four halogens unite with hydrogen. The affinity toward this element decreases as the atomic weights increase. Thus, hydrogen and fluorine unite explosively at low temperatures and in the dark (heat of formation of 1 gram-molecular weight of HF at 18° [1 atmosphere] = 63,991 calories), whereas hydrogen and iodine (solid) unite by a reversible reaction with the absorption of heat (-5926 calories). (See Hydrogen Iodide.) The hydrides of the halogens are all colorless gases.

The affinity of the halogens for oxygen increases as the atomic weight increases. Thus, iodine pentoxide is a well-defined crystalline solid while chlorine monoxide, peroxide and heptoxide are very unstable even at ordinary temperatures. Oxides of fluorine and bromine are unknown. When treated with water, the oxides of the halogens yield acids, thereby indicating that the simple halogens are non-metals.

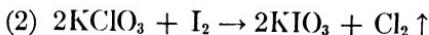
In combination with hydrogen or the metals, the halogens are univalent and negative. When combined with oxygen or in the form of their oxygen salts, they have valences that are often greater than 1 and are positive. Of the halogens, fluorine exhibits the most marked tendency to become negative and the greatest antipathy toward becoming positive, whereas iodine shows the greatest inclination to become positive and the least to become negative.

A halogen of lower atomic weight will displace one of higher atomic weight from its binary hydrogen compounds or from the salts thereof (1).



This shows that the force with which the respective halogens hold electrons diminishes from fluorine to iodine.

On the other hand, a halogen of higher atomic weight will displace one of lower atomic weight from halogen oxyacids or their salts. Thus, iodine will liberate chlorine from potassium chlorate (2) or from perchloric acid.



Fluorine exhibits some peculiar differences from the other members of this family. For example, silver chloride, bromide and iodide are nearly insoluble in water, whereas silver fluoride is appreciably soluble. Sodium chloride, bromide and iodide are readily soluble in water, whereas sodium fluoride is much less soluble.

### FLUORINE<sup>1,2</sup>

Symbol, F. Valence, 1. Atomic Weight, 19; Atomic Number, 9

**History.**—In 1886, Moissan, a French chemist, succeeded in isolating fluorine by the electrolysis of anhydrous hydrofluoric acid in molten potassium hydrogen fluoride. In 1860, Gore succeeded in liberating small quantities of the gas by heating potassium fluoplumbate (1). The addition of fluorspar,  $\text{CaF}_2$ , to various minerals for the purpose of facilitating their fusion was recorded by both Basil Valentine in the fifteenth century and by Agricola in the sixteenth century. The fact that fluorspar had been used for centuries as a flux was no doubt responsible for naming the element *fluorine*, which is derived from the Latin *fluo*, "to flow."



**Occurrence.**—The great activity of this element would preclude its occurrence as such in Nature. However, it is claimed that minute traces of free fluorine have been detected. In combination, its principal minerals are *fluorite* or *fluorspar* [ $\text{CaF}_2$ ], *apatite* or *fluorapatite* [ $\text{CaF}_2 \cdot 3\text{Ca}_3(\text{PO}_4)_2$ ], and *cryolite* [ $\text{AlF}_3 \cdot 3\text{NaF}$ ]. The first two minerals are widely distributed while the latter is found in large deposits in Greenland and Iceland. The bones and enamel of teeth of mammals contain small amounts of calcium fluoride.

Fluorine is the seventeenth most plentiful element in the earth's crust which places it below chlorine but above bromine.

**Physical Properties.**—Fluorine is a pale yellow gas having a characteristic odor resembling a mixture of ozone and chlorine. It may be condensed to a pale yellow liquid, boiling at  $-187^\circ \text{C}$ . Solid fluorine melts at  $-223^\circ \text{C}$ .

**Chemical Properties.**—Fluorine is an intensely active substance, if not the most active element known. It combines directly with

<sup>1</sup> Fluorine Chemistry, Chem. Ind., **59**, 1006, (1946).

<sup>2</sup> Chemical Uses Promising for Fluorine, Ind. and Eng. Chem., News Ed., **25**, 43, (1947); see also J. Chem. Ed., **24**, 314 (1947).

all of the elements excepting oxygen, nitrogen, chlorine, and the inert gases (helium family). All organic compounds are attacked by it. Hydrogen, sulfur and many other elements ignite spontaneously in an atmosphere of fluorine. Ordinary illuminating gas is ignited by it, hence the use of a stream of illuminating gas to detect leaks in a fluorine apparatus. Most metals unite with it to form fluorides. Gold and platinum do not react with it below red heat. Fluorine abstracts hydrogen from its compounds. It decomposes water to form hydrofluoric acid and ozone (2).



**Commercial Manufacture.**—The electrolytic generation of fluorine is possible under varying conditions of temperature and electrolyte composition. One commercially practical cell of the diaphragm type draws approximately 1000 amperes. Ordinary carbon steel is used for the major parts, including the cell body, the hot water jacket, the HF feed line, the cathode, and the solid part of the diaphragm. The anodes are carbon rods impregnated with copper and the diaphragm is a Monel screen. The electrolyte is fused KF·2HF to which has been added 1 to 1.5 per cent LiF. The cell operates at 95° to 115° C. with an anode current efficiency close to 95 per cent and an overall potential drop of 9 volts. These cells can operate continuously for more than a year and produce 99 per cent fluoine after removal of 4 to 8 per cent HF.

Prior to 1942, only a few pounds per day of fluorine were produced. During World War II the demand for fluorine increased, so that by 1945 production was measured in tons per day.

Fluorine gas can be handled satisfactorily at ordinary temperatures and atmospheric pressure in piping, tubing, and other vessels constructed of copper, steel, nickel and Monel.

**Uses.**—In the organic field, simple fluorine-containing compounds have been used for more than a decade as refrigerants, known as *Freon*. These are good solvents and dispersants for aerosol insecticides. Fluorocarbons, because of their extreme stability, are used as lubricants and inert solvents. Sulfur hexafluoride is finding its principal application as a gaseous dielectric in high-voltage generators.

#### NON-OFFICIAL COMPOUNDS OF FLUORINE

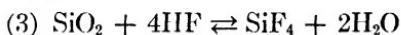
**Hydrogen Fluoride and Hydrofluoric Acid.**—Scheele discovered what is possibly the most important compound of fluorine, *viz.*, hydrogen fluoride. In 1808, Gay-Lussac and Thenard prepared the anhydrous compound, which is a colorless, fuming liquid, boiling at 19.4° C. and freezing at -92.3° C. It is miscible in all proportions with water and, like the other halogen acids, gives on distillation an acid having a constant boiling-point of 120° C. (760 mm.) and containing 35 per cent of hydrogen fluoride. Vapor density determinations indicate that hydrogen fluoride molecules

combine to form complex aggregates. Simons and Hildebrand believe that at ordinary temperatures hydrogen fluoride consists of a mixture of HF and  $H_6F_6$  in equilibrium,  $6HF \rightleftharpoons H_6F_6$ . A rise in temperature causes the dissociation of  $H_6F_6$  into 6HF, while conversely, a reduction in temperature effects an association of 6HF into  $H_6F_6$ .

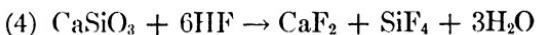
Hydrogen fluoride gas is poisonous and the liquid hydrogen fluoride or its solutions are very corrosive, producing slow-healing wounds when dropped on the skin.

Hydrofluoric acid behaves very much like the other halogen acids, especially hydrochloric acid. Metals, *e. g.*, lead and zinc, are not as readily attacked by hydrofluoric acid as they are by hydrochloric acid. Unlike the halogen acids, hydrofluoric acid forms both normal and hydrogen salts, *e. g.*, potassium fluoride (KF) and potassium hydrogen fluoride ( $KHF_2$ ).

The most characteristic chemical property of hydrofluoric acid, *viz.*, its action upon silicon dioxide and silicates, was known as early as the seventeenth century. Hydrofluoric acid acts upon silicon dioxide (sand) to form gaseous silicon tetrafluoride ( $SiF_4$ ) and water (3).

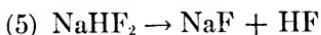


Glass, which is a mixture of silicates, is also attacked by hydrofluoric acid. The fluorides of the metals, silicon tetrafluoride and water are formed according to the representative equation (4).

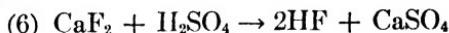


When glass is introduced into an atmosphere of moist hydrogen fluoride, it acquires a rough or "frosted" surface. Glassware, *e. g.*, thermometers, volumetric flasks, etc., can be etched or marked with hydrofluoric acid. First the glass surface is covered with paraffin to localize the action of the acid and then the paraffin is removed with a stylus from such parts of the glass as are desired to be etched.

**Preparation.**—Hydrogen fluoride is prepared by heating dry sodium hydrogen fluoride (5).



*Hydrofluoric Acid.*—Aqueous solutions of hydrogen fluoride can be prepared by distilling a mixture of powdered fluorspar ( $CaF_2$ ) and concentrated sulfuric acid from either a lead or platinum retort (6), and absorbing the evolved hydrogen fluoride in distilled water contained in a lead, paraffin, rubber or bakelite flask. It should be stored in the aforementioned containers because of its action on glass.



*Fluorides.*—The normal salts of hydrofluoric acid are prepared in much the same manner as are the normal salts of the other hydrohalogen acids. As has previously been pointed out (p. 79), the

solubilities of the fluorides are markedly different from those of the salts of the other halogen acids. For example, silver fluoride is appreciably soluble, whereas silver chloride, bromide and iodide are nearly insoluble. Furthermore, sodium fluoride is much less soluble than sodium chloride, bromide and iodide.

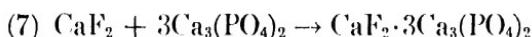
Sodium fluoride ( $\text{NaF}$ ) is in the U. S. P. XIII as a reagent chemical and potassium fluoride ( $\text{KF} \cdot 2\text{H}_2\text{O}$ ) is similarly listed in the N. F. VIII.

**Pharmacology of the Fluoride Ion.**—The fluoride ion is notably toxic. It is thought that this property is occasioned by the formation of insoluble calcium fluoride. Sodium fluoride is a general protoplasmic poison. It is also an excellent antiseptic, and as such has been used as a preservative and to prevent fermentation (beer, 0.01 to 0.015 Gm. per liter).

Fluorine in the form of sodium fluoride or sodium silicofluoride is used in aqueous solution (1 per cent) as a spray to moth-proof clothing. The spray is also effective against ants, roaches and other insects. In the form of a dusting powder (95 per cent  $\text{NaF}$ ) it has long been used to combat chicken lice. Sodium fluoroacetate, commercially known as 1080, is being used as a very effective rodenticide. The administration of very small quantities of sodium fluoride results in the deposition of calcium fluoride, in the bones, which become unusually hard and brittle.

Certain fluoride salts, notably calcium and sodium fluoride, have recently become of importance in dental practice<sup>1</sup> for retarding or preventing dental caries. The fluoride may be applied in solution directly to the tooth enamel by means of a swab or dissolved in the drinking water. In drinking water sodium fluoride is used in concentrations of 1 or 2 parts per million. Too much fluorine in the body leads to mottled or otherwise affected teeth.

A commercial preparation, Enziflur Lozenges, contains calcium fluoride, and vitamins C and D. The fluoride is thought to combine with calcium and phosphorus in the teeth to form fluorapatite (7).



<sup>1</sup> J. Am. Dent. Assoc., **34**, 26 (1947); ibid., **34**, 719 (1947); J. A. M. A., **136**, 112 (1948); Drug and Cos Ind., **61**, 611 (1947).

## CHAPTER VI

### CHLORINE

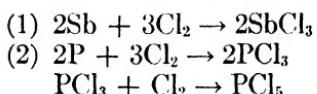
Symbol, Cl. Valence, 1. Atomic Weight, 35.457; Atomic Number, 17

**History.**—This gaseous chemical element takes its name from Greek, *χλωρός*, meaning “greenish yellow.” Scheele discovered it in 1774 and called it “dephlogisticated muriatic acid.”<sup>1</sup> In 1785, C. L. Berthollet expressed his belief that it was a compound of oxygen and hydrochloric acid and named it “oxygenized muriatic acid.” In 1810-1811, Sir H. Davy proved conclusively that it was an element and gave it the name *chlorine*.

**Occurrence.**—Chlorine never occurs as such in Nature. In combination with the alkali metals it occurs widely distributed as *rock salt* ( $\text{NaCl}$ ), as *carnallite* ( $\text{KCl} \cdot \text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ ), and as *sylvite* (native  $\text{KCl}$ ) at Stassfurt. It is found in combination with the alkali metals in sea salt, in various spring waters, and in the tissues of plants and animals. Sea water contains about 2.07 per cent of combined chlorine. Volcanic gases contain chlorine in the form of hydrochloric acid (*q. v.*).

**Physical Properties.**—Chlorine is a greenish yellow gas, having a characteristic unpleasant, suffocating odor and an astringent taste. The vapor density of chlorine is 2.4885 (air = 1). Its critical temperature is  $144^\circ \text{ C}$ . and its critical pressure 76 atmospheres. Its vapor pressure at  $20^\circ \text{ C}$ . is 4993 mm. of mercury or 6.62 atmospheres. It can be liquefied at  $-34.6^\circ \text{ C}$ . under atmospheric pressure and at ordinary temperatures by compression. It solidifies and crystallizes at  $-102^\circ \text{ C}$ . Two hundred and fifteen cubic centimeters of the gas dissolve in 100 cc. of water at  $20^\circ \text{ C}$ . It is only slightly soluble in a concentrated solution of sodium chloride.

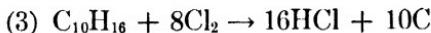
**Chemical Properties.**—At ordinary temperatures, chlorine unites directly with many other elements. In direct sunlight, or in the actinic light of burning magnesium, it combines explosively with hydrogen. Powdered arsenic, antimony, copper, and phosphorus ignite spontaneously in an atmosphere of chlorine to form the corresponding chlorides (1 and 2).



It does not combine directly with carbon, nitrogen, and oxygen. Many compounds containing hydrogen are readily decomposed by chlorine. For example, if a few drops of hot turpentine are placed upon a strip of paper and then immersed in an atmosphere of

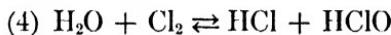
<sup>1</sup> Stahl and others regarded the hypothetical principle of combustion as an element. Carbon and sulfur were thought to be nearly pure phlogiston.

chlorine, a violent reaction takes place with the formation of hydrochloric acid and carbon (3).

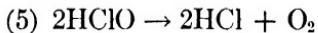


Furthermore, a lighted taper burns in chlorine with a very luminous flame. Therefore, it may be concluded that chlorine does not readily unite with carbon.

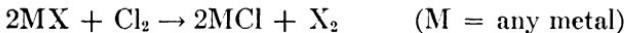
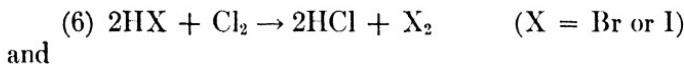
A saturated solution of chlorine in distilled water (Chlorine Water) is listed among the Test Solutions of the U. S. P. XIII. A freshly prepared solution of chlorine in water was official as Aqua Chlori in U. S. Pharmacopœia, 1890. It has a yellow color, which disappears on standing. This is caused by the action of chlorine upon water to form hydrochloric and hypochlorous acids (4), both of which are colorless.



In a one-half saturated chlorine water at 10° C., 33 per cent of the chlorine is changed to hydrochloric and hypochlorous acids. The equilibrium thus established is readily destroyed by the action of light on hypochlorous acid forming hydrochloric acid and oxygen (5).



Consequently, in an effort to reestablish the equilibrium, more chlorine reacts with water according to equation (4). In the presence of light these reactions continue until the colorless solution contains only a small quantity of dissolved chlorine. Freshly prepared chlorine water contains free chlorine, hydrochloric acid, and hypochlorous acid. In order to retain as much chlorine *per se* in solution as possible, chlorine water should be kept in a dark place. As stated previously, chlorine has the property of displacing halogens of higher atomic weight from the hydrogen halides or their salts (6).



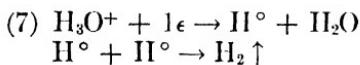
When water at 0° C. is saturated with chlorine, a pale green compound, chlorine hydrate ( $\text{Cl}_2 \cdot 8\text{H}_2\text{O}$ ), crystallizes out. At higher temperatures this compound is readily decomposed into its constituents. Chlorine hydrate is of historical interest because, in 1823, Faraday prepared the first liquid chlorine by placing this compound in one arm of a U-tube, sealing the open end and placing the empty limb in a freezing mixture. When the hydrate was warmed gently chlorine was driven off and liquefied by its own pressure in the empty part of the tube.

**Tests for Identity.**—1. Free chlorine may be recognized by its characteristic odor.

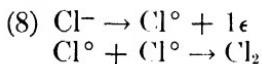
2. It liberates iodine from solutions of potassium iodide (6).
3. Litmus, indigo, etc., are bleached by chlorine.
4. Chlorine acts as a powerful oxidizing agent.

**Commercial Manufacture.**—Chlorine is made by the electrolysis of sodium chloride or potassium chloride.

1. *The Electrolytic Manufacture.*<sup>1</sup>—This method of preparation not only produces chlorine but also hydrogen and sodium hydroxide (potassium hydroxide if KCl replaces NaCl). Sodium chloride in aqueous solution will ionize into sodium ions,  $\text{Na}^+$ , and chloride ions,  $\text{Cl}^-$ . The water will supply hydronium ions,  $\text{H}_3\text{O}^+$ , and hydroxide ions,  $\text{OH}^-$ . The passing of an electric current through such a solution causes the positively charged ions ( $\text{Na}^+$  and  $\text{H}_3\text{O}^+$ ) to travel toward the cathode, whereas the negatively charged ions ( $\text{Cl}^-$  and  $\text{OH}^-$ ) migrate toward the anode. Being a much more reactive element than hydrogen, sodium requires a higher voltage to accept an electron and thus convert the sodium ion to sodium atom.<sup>2</sup> The voltage may be regulated so that the hydronium ion does accept an electron and thus liberates hydrogen (7).



The liberation of chlorine at the anode rather than  $\text{OH}^-$  ions liberating an electron takes place at the same time and in a similar manner (8).



The chlorine is removed, dried and compressed in steel cylinders to a liquid.

The aqueous solution remaining after electrolysis contains sodium hydroxide which is obtained by evaporating the solution to dryness. This residue is purified and fused into sticks or pellets (see p. 190).

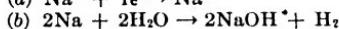
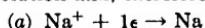
**Laboratory Preparation.**—Place 5 Gm. of potassium permanganate crystals in a flask provided with a dropping funnel and with washing and drying bottles. Twenty-five cubic centimeters of Hydrochloric Acid, U. S. P., previously diluted with an equal quantity of water, is allowed to fall drop by drop from the dropping funnel upon the permanganate (9).



Any hydrogen chloride carried over is condensed in about 50 cc. of water contained in the washing bottle and the chlorine is dried by passing it through concentrated sulfuric acid in a drying bottle. The chlorine is collected by upward displacement of the air in a suitable jar.

<sup>1</sup> Paper Trade J., 109, 86 (1939).

<sup>2</sup> An alternative explanation is that the sodium ion migrates to the cathode and accepts an electron, thus becoming sodium metal (a) which, of course, cannot exist as such in an aqueous solution and, therefore, forms  $\text{NaOH}$  and  $\text{H}_2$  (b).



The formation of chlorine is the simple giving up of an electron to the anode (8).

Chlorine may also be prepared by heating 25 cc. of U. S. P. Hydrochloric Acid previously diluted with 25 cc. of water, with 10 Gm. of manganese dioxide. The evolved gas is washed and dried in the same manner as described above.

If chlorine water is desired, the drying bottle containing the concentrated sulfuric acid may be omitted and the washed gas passed directly into 400 cc. of distilled water kept at a temperature not above 10° C. until a saturated solution is obtained.

**Pharmacological Action of Chloride Ion.**—The chloride ion ( $\text{Cl}^-$ ) has practically no pharmacological action. Chloride ions, together with sodium ions, are necessary for the osmotic function which they perform. The extracellular fluid of the body contains about 0.17 per cent of dissociated sodium chloride. This concentration is maintained through the agency of the skin and urine, which either give off or retain sodium chloride, depending upon the increase or decrease of its intake.

Acidosis may be caused by an excess of the chloride ion in the body. (See Ammonium Chloride, p. 272.) Chlorine as such is rarely employed in medicine but has been recently used when greatly diluted with air as an inhalant in treating infections of the sinuses and bronchi. Preparations which liberate free chlorine are widely used as germicides and deodorizing agents.

**Pharmaceutical Preparations and Uses.**—1. *Chlorine Test Solution* (Chlorine Water), U. S. P. XIII.—This is a saturated solution of chlorine in distilled water (see p. 84). Chlorine in solution is very irritating and caustic.

2. *Sodium Hypochlorite Solution* (Liquor Sodii Hypochloritis), U. S. P. XIII.—(See p. 194.)

3. *Diluted Sodium Hypochlorite Solution* (Liquor Sodii Hypochloritis Dilutus, Liquor Soda Chlorinatae Chirurgicalis, Surgical Solution of Chlorinated Soda, Modified Dakin's Solution), N. F. VIII.—(See p. 194.)

4. *Hyclorite*, N. N. R., is a solution of chlorinated soda, each 100 Gm. of which contains sodium hypochlorite 4.05 Gm., sodium chloride 2.5 Gm., calcium hydroxide 0.14 Gm., and 0.65 Gm. of inert salts. It contains not less than 3.85 per cent of available chlorine. One volume of Hyclorite diluted with 7 volumes of water has the same available chlorine content as "diluted sodium hypochlorite" solution and is isotonic. The degree of alkalinity is less than the official hypochlorite solution and has more available chlorine. They are both used similarly in medical practice. (See N. N. R., 1947, pp. 85, 568.)

5. *Bleaching Powder* (Chlorinated Lime) was recognized by the U. S. P. XI under the Reagent Standards. (See p. 338.)

6. *Chlorinated Paraffin* (Paraffinum Chlorinatum, Chlorcosane), N. F. VIII.—Chlorinated Paraffin is a light yellow to light amber, clear, thick, oily liquid. It is odorless, and is stable in air. It is made by treating liquid paraffin with chlorine. It is used as a solvent for dichloramine-T. Its chlorine is not active, hence chlorinated paraffin is not antiseptic.

7. *Chloramine-T* (Chlorammina-T, Chloramine), N. F. VIII.—This white or faintly yellow, crystalline organic compound of chlorine contains the equivalent of not less than 11.5 per cent and not more than 13 per cent of active chlorine (Cl). Active chlorine is often referred to as "available chlorine" and is that chlorine which is liberated from a substance when treated with an acid.

Chloramine-T has a slight odor of chlorine, is affected by light, and slowly loses chlorine upon exposure to air. One Gm. is soluble in 7 cc. of water at 25° C. and in about 2 cc. of boiling water. It is insoluble in ether and in chloroform. Alcoholic solutions decompose on standing.

It is less irritating than NaOCl, dissolves necrotic tissue only slightly, and therefore is usually used in 1 to 2 per cent aqueous solution to prevent reinfection of wounds. Its effectiveness is obviously due to the slow liberation of chlorine.

8. *Chloroazodin* (Chloroazodinum, Azochloramid), U. S. P. XIII.—This compound contains the equivalent of not less than 37.5 per cent and not more than 39.5 per cent of active chlorine (Cl). It occurs as bright yellow needles or flakes, has a faint odor suggestive of chlorine, and a slightly burning taste. Glycerin and alcohol solutions decompose rapidly on warming and all solutions decompose on exposure to light. It is very slightly soluble in water and in chloroform, sparingly soluble in alcohol and slightly soluble in glycerin and in triacetin. Chloroazodin explodes when heated to 155° C. and decomposition is accelerated by contact with metals.

9. *Chloroazodin Solution* (Liquor Chloroazodini), U. S. P. XIII.—This compound contains not less than 0.24 Gm. and not more than 0.28 Gm. of  $C_2H_4Cl_2N_6$ . Glyceryl triacetate is used as the solvent. This is considered superior to solution of Dichloramine-T or Dakin's Solution because of the slow and steady way in which its chlorine is liberated. It has gained great popularity in England. The solution should be preserved in tight, light-resistant containers and it should not be permitted to come in contact with metals.

10. *Succinchlorimide* (Succinchlorimidum), N. F. VIII.—The chlorinated imide of succinic acid occurs as a white, crystalline powder with the odor and taste of chlorine. Succinchlorimide contains not less than 25 per cent and not more than 27 per cent of active chlorine. One gram is soluble in 70 cc. of distilled water and the solution is acid to litmus. It is sparingly soluble in chloroform and carbon tetrachloride.

It is used principally for disinfecting water. A concentration of about 1:100,000 is effective against *Eberthella typhi*, *Salmonella paratyphi*, and other infectious bacteria.

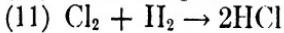
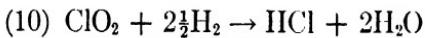
Succinchlorimide Tablets, N. F. VIII, are available for use.

11. *Halazone*, N. N. R., is p-sulfonedichloramido benzoic acid. It occurs as a white powder having a strong odor of chlorine. Halazone should contain not more than 26.26 per cent and not less than 24 per cent of active chlorine. It is stable in solid form and is slightly soluble in water and in chloroform. The acid group present allows salt formation with alkalies. When used with

alkali carbonates, borates or phosphates, halazone in concentrations of 1 in 200,000 to 1 in 500,000 will sterilize water. It is effective against the same organisms as succinchlorimide.

**Other Uses.**—Since the early part of the century chlorine has been used to purify the drinking water of our cities. Long before this, however, chlorine was known to prevent putrefaction and remove the odor of decay. The most important use of chlorine today is in water purification.<sup>1</sup> Water is treated with an excess of gaseous chlorine and then carbon is added which adsorbs certain objectionable impurities and reduces the chlorine concentration to 0.2 part per 1,000,000. The water-carbon mixture is then filtered. Some chlorine is allowed to remain in the water to protect it while moving through the mains. Chlorinated water is often unpalatable due to chlorine compounds formed from the impurities. Phenolic compounds, for example, will be converted to chlorphenols which have a characteristic unpleasant taste and odor. Algae growth in water presents a similar difficulty.

Recently, chlorine dioxide ( $\text{ClO}_2$ )<sup>1</sup> has been used to purify drinking water and besides having two and a half times the oxidizing power of chlorine does not chlorinate contaminating compounds (10, 11), but oxidizes them to odorless and tasteless products.



Chlorine dioxide is a good bactericide, but it is not economical to use it for sterilizing drinking water. Therefore, to purify drinking water, chlorine is first added to disinfect it and then chlorine dioxide to destroy unpleasant tastes and odors.

Chlorine dioxide is also the best compound for bleaching flour, fats, oil, paper, textiles, etc. Its action is instantaneous and does not weaken the fiber of materials.

<sup>1</sup> J. Chem. Ed., 22, 283, (1945).

## CHAPTER VII

### BROMINE

Symbol, Br. Valence, 1. Atomic Weight, 79.916;  
Atomic Number, 35

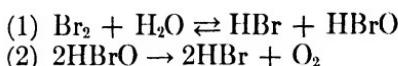
**History.**—In 1826, A. J. Balard isolated this element from the concentrated mother liquor of the salines of Montpellier. He named it *bromine* (Greek,  $\beta\rho\omega\mu\sigma$ , a stench) because of its pungent, unpleasant smell. Prior to its discovery, Joss had confused it with selenium and Liebig thought that it was chlorine. Balard's investigations established the elemental character of the substance and demonstrated that its chemical properties were very similar to those of chlorine and iodine.

**Occurrence.**—Bromine does not occur in Nature in the uncombined condition, but is always united with various metals. The mineral *bromyrite* ( $\text{AgBr}$ ) is naturally occurring. Sodium, potassium, calcium and magnesium bromides are found in mineral waters (kissingen, kreuznach, etc.), in river and sea water, and occasionally in marine plants and animals. Its principal commercial sources are: (a) Sea water (0.007 per cent  $\text{MgBr}_2$ ); (b) Dead Sea (9 per cent  $\text{MgBr}_2$ ); (c) the carnallite deposits at Stassfurt in Prussian Saxony, where, after the extraction of the potassium chloride from the impure mineral, the mother liquor is found to contain appreciable quantities of magnesium and sodium bromides; and (d) the brines of Michigan, Ohio, Pennsylvania, Kentucky, and West Virginia. These brines contain about 25 per cent solids and 1300 parts per 1,000,000 of bromine. In the form of bromides, it is also found in small quantities in the mother liquors from kelp and Chile saltpeter.

**Physical Properties.**—At ordinary temperatures, bromine is a dark reddish-brown mobile liquid, which in any quantity appears almost black. It has a density of 3.19, and boils at  $58.78^\circ \text{C}.$ , forming a deep red, poisonous vapor which is very irritating to the respiratory organs. At ordinary temperatures, it has a high vapor pressure (150 mm. at  $18^\circ \text{C}.$ ) and hence evaporates very quickly. When cooled to  $-21^\circ \text{C}.$ , it forms red, needle-shaped crystals (melting-point,  $-7.3^\circ \text{C}.$ ). One Gm. of bromine dissolves in about 30 cc. of water at  $20^\circ \text{C}.$ , and is freely soluble in alcohol, ether, chloroform and carbon disulfide. Alcohol and ether are gradually decomposed by bromine, forming bromine substitution products.

**Chemical Properties.**—In general, the chemical properties of bromine are intermediate between those of chlorine and iodine (*q. v.*). It does not combine directly with oxygen, nitrogen, or carbon, and will unite with hydrogen only in the presence of a catalyst or

at fairly high temperatures (heat of formation of HBr = 8600 calories). Bromine unites directly with the non-metals (phosphorus, arsenic, etc.) and also with most of the metals. When a metal is heated and held in bromine vapor, it bursts into flame. In the presence of sunlight, hydrobromic and hypobromous acids are formed in aqueous solutions of bromine (1). The hypobromous acid is further decomposed into hydrobromic acid and free oxygen (2).



**Tests for Identity.**—1. Bromine may be recognized by its characteristic, unpleasant odor.

2. It destroys organic matter and bleaches litmus, indigo and other coloring materials.

3. It imparts a yellow color to starch test solution.

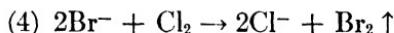
4. When an aqueous solution of bromine is shaken with carbon disulfide, the latter acquires a reddish yellow color.

**Commercial Manufacture.**—The methods of bromine preparation depend upon the oxidation of the bromide ion to elemental bromine.

1. *Recovery From Sea Water.*<sup>1</sup>—Sea water contains 3.5 per cent total solids and 65 to 70 parts per 1,000,000 of bromine. The total solids and 65 to 70 per cent per 1,000,000 of bromine. The sea water is acidulated with sulfuric acid (0.27 pound of 96 per cent  $\text{H}_2\text{SO}_4$  per ton of sea water) to a pH of about 3.5. This is necessary because if the sea water is just brought to neutrality and then chlorine added, the following reaction will take place (3):



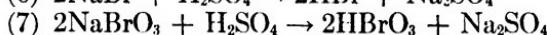
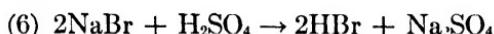
The excess sulfuric acid causes the reaction to remain completely on the left-hand side due to the hydrogen ions released from the sulfuric acid. Chlorine is passed through the acidulated sea water to oxidize the bromide to free bromine (4).



The bromine thus generated is blown out of the solution and absorbed by a sodium carbonate solution to concentrate the bromine as sodium bromide and bromate in a small volume (5).



The solution of bromide and bromate so obtained is treated with sulfuric acid (6, 7 and 8). The bromine vapors are then steamed out of the acidified solution and are condensed to pure liquid bromine.



<sup>1</sup> Ind. Eng. Chem., 21, 434 (1929); 26, 361 (1934).

2. *Recovery From the Dead Sea and From Natural Bromide-containing Brine.*—The procedure is the same as that used for sea water except acidification with sulfuric acid is unnecessary.

3. *Electrolysis.*—Bromine may be obtained by the electrolysis of bitters. These aqueous solutions of various bromides and chlorides yield upon electrolysis free bromine until all of the bromides have been decomposed. During the operation, chlorine is also liberated from the chlorides present, but it immediately displaces the bromine from its salts and becomes fixed. The current is stopped as soon as chlorine begins to come off.

**Pharmacological Action of the Bromide Ion.**—The fact that psychic functions and the reflexes are depressed by inorganic bromides, whereas in general organic bromine compounds and bromates do not act in this manner, has led to the conclusion that these effects are due to the bromide ion. According to Frey, the bromide ion is distributed similarly in the body to the chloride ion (*q. v.*) and which it partially displaces in the blood, gastric juice, etc. The administration of fairly large doses of bromides tends toward the production of mental calm and the elimination of worry, which action, if not resisted, is conducive to rest and sleep. Bromides are in no sense anodynes or hypnotics. The long-continued use of bromides may produce psychic weakness, poor memory, apathy, sexual impotency, and malnutrition. Bromide rashes (bromism) are not uncommon, especially in cases of prolonged administration of large doses. Bromides have been replaced largely by phenobarbital and sodium diphenyl hydantoinate (Dilantin) in the treatment of epilepsy. Bromides are eliminated chiefly by the urine.

**Uses.**--Bromine is used in making bromides for medicinal purposes, in analytical chemistry, in photography, and in the preparation of organic dyes. It is a very irritant poison and a powerful escharotic and is, therefore, rarely used in medicine. Irritation of the respiratory tract caused by bromine may be relieved by inhalations of alcohol vapor.

Bromine Water is included in the list of Test Solutions given in the U. S. P. XIII. It is a saturated solution of bromine prepared by agitating from 2 to 3 cc. of bromine with 100 cc. of cold distilled water in a glass-stoppered bottle, the stopper of which should be lubricated with petrolatum. It is to be preserved in a cool place, protected from light.

Bromine is listed among the Reagent Standards of the U. S. P. XIII. Standards for its quality, *i. e.*, specific gravity, limits for non-volatile matter, organic bromine compounds, iodine, and sulfur compounds are specified and appropriate tests given.

## CHAPTER VIII

### IODINE

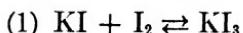
*Iodine*, U. S. P. XIII

Symbol, I. Valence, 1. Atomic Weight, 126.92;  
Atomic Number, 53

**History.**—The name of this solid halogen element was derived from the Greek, *ἰωδης* (violet colored), in allusion to the color of its vapor. While investigating the products obtained from the mother liquor prepared by lixiviating kelp or the ashes of seaweeds, B. Courtois, a soap boiler of Paris, discovered iodine in 1812. Three years later L. J. Gay-Lussac studied its properties and showed it to be an element. It was first introduced into medicine in 1819 by Coindet.

**Occurrence.**—Iodine does not occur as such in Nature, but is found widely but sparingly distributed in the form of iodides and iodates, chiefly of potassium and sodium. Small quantities are also found in some minerals in combination with silver, lead, mercury and other metals. Sea water, seafoods, seaweed and sponges contain small quantities of iodides. The ashes obtained by burning seaweeds are known in Scotland as kelp; in Norway as varec; and in Spain as barilla. They often contain as much as 2 per cent of iodine as iodides, etc. Iodine also occurs in the thyroid glands of animals in organic combination as a part of thyroxin. Chile salt-peter (impure sodium nitrate) contains approximately 0.2 per cent of a mixture of sodium iodide and sodium iodate.

**Physical Properties.**—Iodine occurs in the form of a grayish black solid, having a metallic luster and a characteristic penetrating odor. It crystallizes in large rhombic plates or granules. At ordinary temperatures it volatilizes slowly and when heated to 114° C., it melts, giving off violet colored vapors. The liquid boils at 183° C. It has a density of 4.93. One Gm. of iodine is soluble in about 2950 cc. of water, in 13 cc. of alcohol, in about 80 cc. of glycerin, and in about 4 cc. of carbon disulfide. Solutions of iodides, *e. g.*, potassium iodide, dissolve large quantities of iodine because of the formation of definite compounds (1).

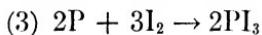


Iodine gives brown solutions with all solvents, except carbon disulfide, carbon tetrachloride and chloroform (violet). It is thought that the brown color of solutions of iodine in certain solvents is due to the products of a weak combination of iodine with these solvents, and that the violet-colored solutions represent iodine in solution in an uncombined form.

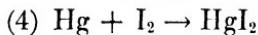
**Chemical Properties.**—The chemical properties of iodine closely resemble those of chlorine and bromine. As a rule, its affinity for other elements, however, is less than that of either. The molecular weight of iodine (by vapor density method from 184° to 700° C.) is 253.8; hence its molecular formula,  $I_2$ . At 1700° C. the dissociation of the diatomic iodine molecule into monatomic molecules is complete and its molecular weight is equal to its atomic weight (2).



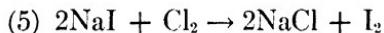
In aqueous solutions, iodine acts as an oxidizing agent. Iodine, even when heated, unites very slowly with hydrogen, the presence of a catalyst (platinum black) being necessary to effect the combination. It combines directly with some non-metals and with the majority of the metals. For example, yellow phosphorus melts and then inflames when mixed with iodine (3); antimony burns in iodine



vapor; and mercury when heated combines rapidly with it (4).



Iodine is displaced from combination with hydrogen and the metals by both chlorine and bromine (5).

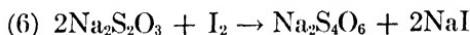


The action takes place either in the dry form or in solution.

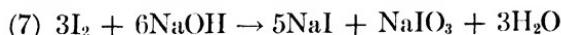
**Official Tests for Identity.**—1. Iodine can be readily detected by the blue color it immediately gives with starch test solution. The color vanishes when the mixture is boiled, but reappears on cooling, provided the boiling has not been too prolonged.

2. The color of its solutions in the various solvents (*q. v.*).

3. Iodine is readily reduced by many reducing agents, especially sodium thiosulfate (6), complete reduction becoming evident by the loss of the characteristic iodine color.



4. When iodine is added to solutions of the alkali metal hydroxides it undergoes a characteristic reaction (7).



**Commercial Manufacture.**—Iodine is obtained from (1) iodides in oil-well brines, (2) iodides present in the ashes of burned seaweed, or (3) iodates in crude Chile saltpeter (caliche).

1. *Recovery From Iodides in Oil-well Brines.*<sup>1,2</sup>—Iodide is present to the extent of about 0.05 Gm. per liter. The details of the process are not well known but from the patent the iodide ion is oxidized to free iodine. The iodine is then adsorbed on activated carbon or charcoal. The cathode of an electrolytic cell is then made from

<sup>1</sup> U. S. Patent 1,944,423; 2,009,956.

<sup>2</sup> Ind. Eng. Chem., **26**, 376.

this iodine-carbon product and by electrolysis iodine is collected at the anode.

2. (a) *The Action of Manganese Dioxide and Sulfuric Acid on Iodides.*—The sources of iodides are (1) brine wells and (2) burned seaweed producing an ash known as kelp, varec or barilla.

The kelp obtained is lixiviated with water to extract the soluble salts. When the liquid is concentrated, the less soluble salts (chiefly alkali chlorides, carbonates and sulfates) crystallize out and are removed. Sulfuric acid is added to the liquid to decompose any



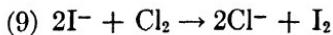
FIG. 8.—Iodine resublimation. (Picture taken at Merck & Co., Inc., by Barrett Gallagher and reprinted from Fortune Magazine by special permission of the editors.)

alkaline sulfides and sulfites present. The sulfuric acid also converts the iodides and bromides into sulfates, and hydrogen iodide and hydrogen bromide are produced and go into solution. Then the liquid is run into the iodine still, warmed, and manganese dioxide is added from time to time (8). The liberated iodine volatilizes and is condensed in suitable receivers.



The iodine thus obtained is purified by mixing it with a small quantity of potassium iodide and subliming. In this way, traces of bromine and chlorine are removed. (See Eq. 1, p. 78.)

(b) *The Action of Chlorine on Iodides.*—A solution containing iodides may be treated with chlorine in a manner similar to that used for obtaining bromine from bromides (see p. 90). When conditions are controlled the following reaction takes place (9).



3. *The Reduction of Sodium Iodate.*—Iodine is obtained in large quantities from the mother liquors of Chile saltpeter, in which it occurs as sodium iodate. When the liquor is mixed in large vats with a calculated amount of sodium bisulfite, iodine is precipitated (10).



Very often the iodine is liberated by the addition of both sodium hydrogen sulfite and normal sodium sulfite (11).

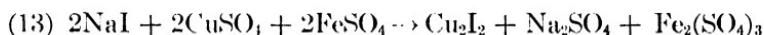


The precipitate is washed and sublimed from iron retorts. (See Fig. 8.)

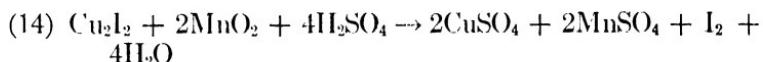
Sometimes the liquors are treated with a sufficient quantity of sodium bisulfite to change the sodium iodate to sodium iodide (12).



When the solution of sodium iodide is treated with cupric and ferrous sulfates, the iodine is precipitated as cuprous iodide (13).



The precipitated cuprous iodide is mixed with manganese dioxide and sulfuric acid and heated. Iodine is liberated and its vapors condensed in a suitable apparatus (14). (See Method 2.)



**Pharmacological Action of the Iodide Ion.**—Iodine when administered internally will be converted to iodide ion regardless of the form of medication. In protein or fat combinations the conversion to iodide is retarded. The iodide ion is similar to chloride and bromide ions in that after absorption it is distributed evenly in the extracellular fluid. The concentration in the saliva or serum is an index to the concentration in all other extracellular fluids. No pharmacological response is noticeable upon the introduction of iodides since the ion does not affect the central nervous system or the circulation.

Its therapeutic use is based on the iodide ion's ability to destroy tissue (histolytic effect) and on its beneficial effect on inflammatory lesions. In tertiary syphilis it has quite a specific action but its use is contraindicated in tuberculous conditions.

Because iodides are stimulating to mucous membrane and are excreted by the bronchial glands, they are useful as expectorants. (See Hydriodic Acid, p. 108.) The loosening of the congestion in sinus disorders is also a result of this action on mucous membrane. (See also p. 199.)

Since iodine is necessary in thyroxin formation, some is required in the diet for proper functioning of the thyroid gland.

**Pharmaceutical Preparations and Uses.**—1. *Iodine* (Iodium), U. S. P. XIII, should contain not less than 99.8 per cent of I. Iodine has been used in medicine for over one hundred years mainly as a counterirritant and disinfectant. Elemental iodine can only exert its characteristic action when used externally. Regardless of whether iodine is administered internally as iodine, a salt of hydriodic acid, or organically combined, it is converted primarily to the iodide ion in the body. The iodide ion is *not* a disinfectant nor a counterirritant, but possesses therapeutically useful characteristics. (See Hydriodic Acid, p. 108, and Sodium Iodide, p. 199.)

2. *Strong Iodine Solution* (Liquor Iodi Fortis, Compound Iodine Solution, Lugol's Solution), U. S. P. XIII.—This solution should contain in 100 cc. not less than 4.5 Gm. and not more than 5.5 Gm. of iodine, and not less than 9.5 Gm. and not more than 10.5 Gm. of potassium iodide. The iodine and potassium iodide are dissolved in 10 cc. of distilled water and then sufficient distilled water added to make 100 cc. The purpose of the potassium iodide is to solubilize the iodine (see p. 92). Since the elemental iodine upon internal administration is promptly converted to the iodide ion, the therapeutic use of Lugol's Solution is that of the iodides. (See Sodium Iodide, p. 199.) Average dose—0.3 cc. (approximately 5 minimis).

3. *Iodine Tincture* (*Tinctura Iodi*, Mild Tincture of Iodine), U. S. P. XIII.—*Note.*—The strength of Iodine Tincture has been reduced from 7 Gm. of iodine in each 100 cc. (U. S. P. XII) to 2 Gm. of iodine in each 100 cc.

This tincture contains, in each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of I and not less than 2.1 Gm. and not more than 2.6 Gm. of NaI. The iodine and sodium iodide are dissolved in a sufficient quantity of diluted alcohol to make the required amount. Sodium iodide<sup>1</sup> is used in preference to potassium iodide because it is believed to react more favorably upon tissue cells. The diluted alcohol is not only a satisfactory solvent but also has the additional advantage of being only slightly irritating when applied to wounds. Furthermore, it will not freeze in cold weather.

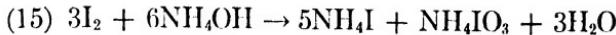
4. *Iodized Oil* (*Oleum Iodatum*), U. S. P. XIII.—This is an iodine addition product of vegetable oils, containing not less than 38 per cent and not more than 42 per cent of organically combined iodine (I). The conversion of the organically combined iodine into the iodide ion takes place slowly within the body. Therapeutically, therefore, it acts as an iodide (p. 95).

5. *Iodides Tincture* (*Tinctura Iodidorum*), N. F. VIII.—*Note:* Iodides Tincture may be dispensed when Decolorized Iodine Tincture is ordered.

This preparation does not contain any iodine as such, but merely the iodides of ammonium and potassium. The iodine (50 Gm.) and alcohol are added to an aqueous solution of potassium iodide

<sup>1</sup> Am. Prof. Pharm., 13, 51, (1947).

(25 Gm.) and the mixture agitated frequently until the iodine is dissolved. Strong ammonia solution (100 cc.) is added and the mixture set aside until it becomes colorless. The reaction is quite complicated and a variety of products are formed. The following is thought to be the main reaction (15).



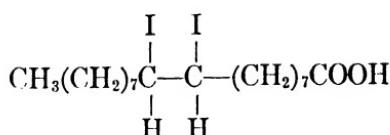
Sufficient alcohol is then added to make 1000 cc. and the product filtered. The preparation was intended as a stainless and colorless external iodine antiseptic. It is a worthless product being no more antiseptic than the water and alcohol which it contains.

6. *Iodine Ampuls* (Ampullæ Iodi, Iodine Swabs), N. F. VIII.—They contain, in each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of I and not less than 2.1 Gm. and not more than 2.6 Gm. of NaI. Each ampul must yield not less than 90 per cent and not more than 110 per cent of the labeled amount of I. The iodine solution in the ampuls is the same as Iodine Tincture, U. S. P. XIII, and has the same use.

7. *Iodine and Zinc Iodide Glycerite* (Glyceritum Iodi et Zinci Iodidi, Diluted Talbot's Solution), N. F. VIII.—The iodine (100 Gm.) is added to a solution of zinc iodide (80 Gm.) in distilled water and the liquid agitated until solution is effected. Then 550 cc. of glycerin, and a sufficient quantity of distilled water, is added to make 1000 cc. Zinc iodide provides the iodide ion necessary for solubilizing the free iodine and also provides the astringent properties for which the preparation is used. The free iodine present makes it an active germicide.

8. *Iodine Ointment* (Unguentum Iodi), N. F. VIII.—*Caution: During its manufacture and storage this ointment must not come in contact with metallic utensils or containers.* Iodine Ointment contains not less than 6.5 per cent and not more than 7.5 per cent of total iodine (I). Iodine (40 Gm.) and potassium iodide (40 Gm.) are triturated with glycerin (120 Gm.) until dissolved. The mixture is incorporated with 800 Gm. of Yellow Ointment (U. S. P. XIII) which is a mixture of yellow wax, wool fat and petrolatum. The ointment possesses good antiseptic properties but is only moderate in counterirritant action. Any absorption of iodine through the skin is very questionable and therefore the use of the ointment with the expectation of systemic iodide effects is unwarranted.

9. *Stainless Iodized Ointment* (Unguentum Iodatum Denigrescens), N. F. VIII.—Iodine (50 Gm.) is dissolved in oleic acid (200 Gm.) with the aid of heat (about 65° C.) (16).



Paraffin (50 Gm.) is added and the heating continued until the reaction is completed (iodine is absorbed or organically combined), as shown by the absence of the reddish color. Petrolatum (700 Gm.) is added and, when liquefied, the product is removed from the heat and stirred frequently until it congeals. The N. F. VIII notes that this ointment improves upon standing for a week or ten days. This is because the chemical reaction between the oleic acid and iodine is more nearly complete. This ointment contains no free iodine (note Iodides Tincture) and thus is void of any antiseptic property. The iodine in organic combination is not absorbed through the skin so no systemic value is possible. Stainless Iodized Ointment has little therapeutic value.

10. *Iodine Solution* (Liquor Iodi), N. F. VIII.—This solution contains, in each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of iodine (I), and not less than 2.1 Gm. and not more than 2.6 Gm. of NaI. It is prepared by dissolving the iodine (20 Gm.) and sodium iodide (24 Gm.) in 50 cc. of distilled water and then making up to 1000 cc. with distilled water. Iodine Solution is a very efficient antiseptic and may be diluted with an equal volume of water without lowering its germicidal properties to any appreciable extent. It has the advantage over Iodine Tincture, U. S. P. XIII, of being less irritating but because no alcohol is present, it dries more slowly. The fact that it freezes in cold weather has prevented it from being widely used. Weak solutions of iodine such as these have been found to be effective antiseptics without having the destructive action upon healthy tissue that results when more concentrated solutions are employed.

11. *Phenolated Iodine Solution* (Liquor Iodi Phenolatus, Boulton's Solution, French Mixture, Carbolized Iodine Solution), N. F. VIII.—Liquefied phenol (6 cc.), strong iodine solution (15 cc.) (U. S. P. XIII), and glycerin (165 cc.) are mixed and sufficient water added to make 1000 cc. The liquid is placed in a strong, tightly-stoppered glass container and either exposed to the sunlight or heated at a temperature not exceeding 70° C. until it becomes colorless or faintly yellow. The facts that the solution is colorless or faintly yellow, and that the solution does not turn blue when starch T.S. is added, show that no free iodine is present in the liquid, it having combined to form tri-ido-phenol and hydriodic acid. Any therapeutic value that this preparation might have is probably due to the phenol and iodo-phenol present. It has been used as a disinfectant and counterirritant, although there is no scientific proof of its efficacy.

12. *Strong Iodine Tincture* (Tinctura Iodi Fortis), N. F. VIII.—*Note: Dispense Strong Iodine Tincture when Tincture of Iodine, U. S. P. XII, is ordered.* This is an alcoholic solution containing in each 100 cc. not less than 6.8 Gm. and not more than 7.5 Gm. of I, and not less than 4.7 Gm. and not more than 5.5 Gm. of potassium iodide. The potassium iodide is dissolved in 50 cc. of distilled water contained in a graduated bottle, the iodine is added,

and the mixture agitated until solution is effected. Sufficient alcohol is added to make 1000 cc. This tincture<sup>1</sup> should not be used as a disinfectant because more damage is usually done to tissue than is warranted by any beneficial results obtained. Large doses (10 to 15 minimis) are sometimes prescribed to be taken in milk, with which it combines chemically to form non-toxic organic iodides and thus has the action of iodides. The only therapeutic value that this tincture might have would be as a counterirritant. This 7 per cent tincture came into vogue in 1840 when it was customary to dissolve 1 ounce of iodine in 1 pint of alcohol.

13. *Calcium Iodobehenate* (Calcii Iodobehenas, Calcium Monoiodobehenate), U. S. P. XIII.—Calcium Iodobehenate consists principally of calcium monoiodobehenate ( $C_{26}H_{42}ICOO$ )<sub>2</sub>Ca and contains, when dried at 100° for 2 hours, not less than 23.5 per cent of I. This organic iodine compound is prepared by treating erucic acid ( $C_{21}H_{44}COOII$ ) with hydriodic acid (III). Erucic acid, an unsaturated fatty acid similar in properties to oleic acid, is found as a glyceride in oil of mustard seed, rape-oil, haddock liver oil and some seed oils. The hydriodic acid thus adds to the double bond of erucic acid forming a saturated acid corresponding to behenic acid ( $C_{21}H_{44}COOII$ ). Its action is due to the slow liberation of iodine forming iodides. Average dose—0.5 Gm. (approximately 7½ grains).

14. *Diluted Hydriodic Acid* (Acidum Hydriodicum Dilutum), U. S. P. XIII.—(See p. 107.)

15. *Hydriodic Acid Syrup* (Syrupus Acidi Hydriodici), U. S. P. XIII.—(See p. 107.)

16. *Ferrous Iodide Syrup* (Syrupus Ferri Iodidi, Sirupus ferrosi iodidi concentratus P.I.), N. F. VIII.—(See p. 613.)

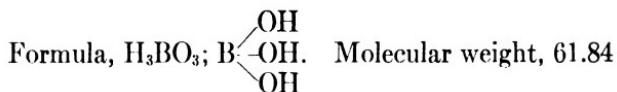
<sup>1</sup> Am. Prof. Pharm., 13, 51 (1947).

# CHAPTER IX

## OFFICIAL INORGANIC ACIDS

### BORIC ACID

*Boric Acid, U. S. P. XIII*



**History.**—In 1702, William Homberg obtained boric acid by heating borax with copperas. Later he prepared it by the action of sulfuric acid upon borax. Until Gay-Lussac and Thenard identified it in 1804 as being an oxygen compound of boron, it was known as Sal Sedativum Hombergi.

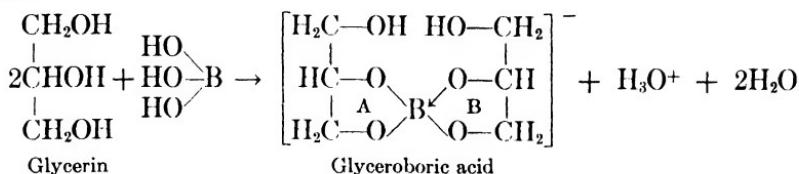
**Occurrence.**—Free boric acid is found in sea water, certain plants and in nearly all fruits. It is likewise found in some volcanic steam jets, notably those in the Tuscany Marshes and the Lipari Islands. It is also present in the natural waters of these regions. By far its largest natural source is in the combined form as, for example,  $Na_2B_4O_7 \cdot 4H_2O$  (rasorite);  $Na_2B_4O_7 \cdot 10H_2O$  (borax);  $CaB_4O_7 \cdot 4H_2O$  (borocalcite);  $H_3BO_3 \cdot Na_2B_4O_7 \cdot 2CaB_4O_7 \cdot 18H_2O$  (tineal); and  $Ca_2B_6O_{11} \cdot 5H_2O$  (colemanite).

**Physical Properties.**—Boric acid is found on the market in three forms: transparent, colorless, odorless, pearly scales having a smooth feel; six-sided triclinic crystals; and white, odorless, rather bulky powder which is unctuous to the touch. All forms are stable in air. The scale and crystalline forms are most suitable for preparing aqueous solutions, because the powder tends to float on top of the water.

At  $25^\circ C.$ , 1 Gm. of boric acid is soluble in 18 cc. of water, in 18 cc. of alcohol, and in 4 cc. of glycerin. One Gm. is soluble in 4 cc. of boiling water and in 6 cc. of boiling alcohol. The addition of HCl decreases its solubility in water. It volatilizes appreciably from aqueous and alcoholic solutions at  $60^\circ C.$  and above.

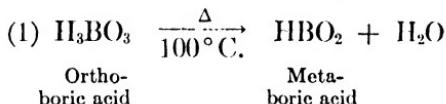
**Chemical Properties.**—Orthoboric acid is a weak acid, its dissociation constant being  $6.5 \times 10^{-10}$  (for the first hydrogen ionized, the others being negligible). It is a tribasic acid, as shown by its esterification to ethyl orthoborate, the vapor density of which corresponds to a molecular formula  $B(OC_2H_5)_3$ . Boric acid cannot be titrated accurately with standard alkali because it is such a weak acid. However, when dissolved in a glycerin solution (official assay) it behaves as a strong monobasic acid which can readily be titrated with standard alkali. The following reaction is thought

to take place to account for the monobasicity of boric acid in glycerin.<sup>1</sup>

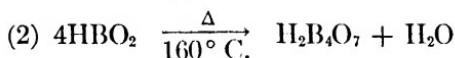


In an analogous manner boric acid enters into combination with other polyhydroxy organic compounds such as glycols and mannitol.

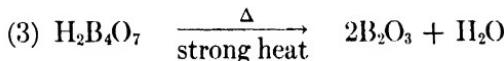
When orthoboric acid is heated at 100° C. or slightly above, it is converted to metaboric acid by loss of a molecule of water (1).



Further heating to approximately 160° C. results in the formation of tetraboric acid (2).



Still further heating converts the residue to boron trioxide, a glassy-appearing solid (3).



**Tests for Identity.**—1. Aqueous solutions impart a claret color to blue litmus paper and a brownish-red color to turmeric paper. The latter turns greenish black upon the addition of ammonia.

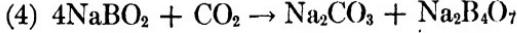
2. An alcoholic solution of boric acid burns with a green bordered flame.

3. When heated to  $100^{\circ}\text{ C}.$ , it decomposes into water and metaboric acid ( $\text{HBO}_2$ ) which in turn is slowly volatilized at that temperature.

4. When heated, boric acid goes through the changes described under Chemical Properties.

5. On account of the non-volatility of the oxide, it will displace most acids from salts when fused with them.

6. Metaborates are unstable and are easily decomposed (4).



**Commercial Manufacture.**—Orthoboric acid is obtained commercially from (1) the decomposition of certain naturally occurring borates and (2) from volcanic steam jets.

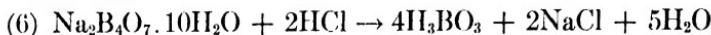
<sup>1</sup> This formulation expresses the currently accepted reaction that takes place between glycerin and boric acid. The arrow indicates a semi-polar bond. The desire of boron to obey the octet rule and borrow another pair of electrons results in a dynamic resonating system of 3 covalent bonds and 1 semi-polar bond. Additional weight is lent to this reaction by the fact that 2 organically stable 5-membered rings (A and B) are formed.

1. Most of the world's supply of boric acid is prepared from the naturally occurring deposits of colemanite, rasanite, borax, etc. For example, colemanite is reduced to a powder, mixed with boiling water, and the suspension is then treated with sulfur dioxide gas to liberate boric acid (5).



When the solution is cooled, the boric acid crystallizes out.

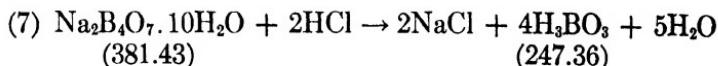
Borax, when treated with HCl, liberates a high grade of medicinal boric acid (6).



The use of HCl, a volatile acid, has superseded that of  $H_2SO_4$  because residual traces of HCl will not remain on the crystal surfaces when they are dried, whereas  $H_2SO_4$ , a non-volatile acid, is less easily removed.

2. Although the foregoing procedures account for most of the world's supply of boric acid, a small amount of *natural* boric acid is obtained from certain volcanic areas in Tuscany and the Lipari Islands. In these areas, volcanic steam jets (*soffioni*) issue from the ground carrying a small amount of vaporized boric acid together with some other gases. These jets are passed into natural or artificially constructed pools of water (*lagoni*) which become highly charged with boric acid. The water from these pools is then concentrated (utilizing the heat of the steam jets) to obtain the crystalline boric acid. More recently, artificial *soffioni* have been bored to increase production.

**Laboratory Preparation.**—Add 50 Gm. of Sodium Borate ( $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ ) to 120 cc. of distilled water and bring the solution to a boil. Filter the boiling solution, and to the filtrate add 30 cc. of Hydrochloric Acid (7). Stir the mixture well and set it aside in a cool place for twenty-four hours or until the next laboratory period. Collect the crystals on a wetted muslin strainer and allow them to drain completely. Wash the crude product with a little cold water and again allow to drain. Weigh the wet mass, dissolve it in approximately five times its weight of boiling distilled water and set the solution aside for two or three days to crystallize. Collect the crystals and wash them with cold water as before, spread them upon bibulous (absorbent) paper and allow them to dry in the air.

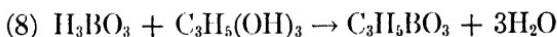


**Pharmaceutical Preparations and Uses.**—1. *Boric Acid* (*Acidum Boricum, Boracic Acid*), U. S. P. XIII.—Boric acid, when dried over sulfuric acid for five hours contains not less than 99.5 per cent of  $H_3BO_3$ . Boric acid is used in solution as a dusting, powder, or incorporated in ointment bases, to allay inflammation and for its mild antiseptic properties. It is generally conceded that boric

acid cannot kill bacteria, but that it will maintain a more or less sterile condition once it has been established by other agents. However, in view of its low value as an antiseptic, and because of its demonstrated toxic nature when taken internally (orally or parenterally) it has been suggested that boric acid be deleted entirely from medicinal use.<sup>1</sup> As proof of its toxic nature one finds many instances recorded in the literature where fatalities have occurred following (1) its intravenous use by error when normal saline solution, etc., is called for; (2) its use orally, again mistakenly, in baby feedings; and (3) application of the ointment over large denuded areas (usually burned) of the skin from which appreciable absorption takes place and produces marked systemic effects. All of these fatal cases exhibited a characteristic color of the skin, the color being most closely described as that of a "boiled lobster."

2. *Kaolin Cataplasma* (*Cataplasma Kaolini*), N. F. VIII.—In addition to other ingredients, this preparation contains 4.5 per cent of boric acid. (See p. 438.)

3. *Boroglycerin Glycerite* (*Glyceritum Boroglycerini*), U. S. P. XIII.—Boroglycerin Glycerite contains not less than 47.5 per cent and not more than 52.5 per cent of boroglycerin ( $C_3H_5BO_3$ ). It is made by dissolving boric acid in glycerin at a temperature between 140° and 150° C. (8). The heating is continued to definite weight and an equal weight of glycerin added. It is used as a dehydrating agent and mild antiseptic. Boroglycerin Glycerite was used to make *Suppositoria Boroglycerini* (*Suppositories of Boroglycerin*), N. F. VII. The glycerite of boroglycerin and the glycerin are mixed well with the melted glycerinated gelatin, poured into well-oiled, slightly warmed moulds of the required size and shape, and allowed to stand until the suppositories are firm.



4. *Boric Acid Solution* (*Liquor Acidi Borici*, Saturated Boric Acid Solution), N. F. VIII.—This solution contains, in each 100 cc., not less than 4.25 Gm. of  $H_3BO_3$ . Fifty Gm. of boric acid are added to 350 cc. of distilled water that has been heated to boiling, the mixture agitated until solution is effected, and then a sufficient quantity of cold distilled water immediately added to make 1000 cc. It is filtered, if necessary, to obtain a clear product.

The National Formulary notes that upon chilling or upon evaporation of the solvent, Boric Acid Solution tends to deposit crystals or become slightly turbid because of the formation of minute crystals of boric acid, which do not readily redissolve except upon heating the solution. Saturated aqueous solutions of boric acid, prepared at any temperature, are quite unstable, in that a reduction of only a few degrees in the temperature of the solution causes the precipitation of the boric acid in crystalline form.<sup>2</sup> These crystals in sus-

<sup>1</sup> J. A. M. A., 129, 333 (1945).

<sup>2</sup> For this reason some manufacturers supply a solution containing not less than 3.5 per cent boric acid.

pension preclude the use of the solution for ophthalmic purposes. The concentration of boric acid in Boric Acid Solution (about 4.25 per cent) is reasonably stable for the usual variations in household temperatures. For external use, the solution may be used undiluted, except for ophthalmic use, for which purpose it may be diluted with an equal volume of sterile distilled water. The dilution of the saturated solution, in addition to guarding against the introduction of crystals into the eye, also renders the solution approximately isotonic, thus minimizing any irritant effect due to a hypertonic solution.

5. *N. F. Antiseptic Solution* (*Liquor Antisepticus N. F.*, Lister's Solution), *N. F. VIII.*—This is a hydroalcoholic solution containing 2.5 per cent boric acid and lesser amounts of thymol, chlorothymol, eucalyptol, methyl salicylate, oil of thyme, and menthol. Its principal use is as an antiseptic mouth wash. The *N. F.* notes that specially denatured alcohol, Formula No. 38-B (100 gallons of ethyl alcohol must contain 6 pounds of boric acid and  $1\frac{1}{3}$  pounds each of thymol, chlorothymol, and menthol), has been approved by the U. S. Treasury Department as suitable for use in this preparation provided that adjustment be made for the quantities of the formula ingredients present in the denatured alcohol. For oral or external use—undiluted.

6. *Compound Zinc Sulfate Powder* (*Pulvis Zinci Sulfatis Compositus*, Antiseptic Powder *N. F. V.*, Soluble Antiseptic Powder), *N. F. VIII.*—This powder contains 86.6 per cent of boric acid and lesser quantities of salicylic acid, phenol, eucalyptol, menthol, thymol, and zinc sulfate (12.5 per cent). It is sometimes used as a dusting powder. More often, its aqueous solution is used as a mild, astrigent, antiseptic douche.

7. *Boric Acid Ointment* (*Unguentum Acidi Borici*, Boracic Acid Ointment), *U. S. P. XIII.*—Boric Acid Ointment contains not less than 9 per cent and not more than 11 per cent of  $H_3BO_3$ . The boric acid is levigated with wool fat to a smooth paste, and then the mixture is incorporated with the white ointment containing wool fat (5 per cent), white wax (5 per cent), and white petrolatum (80 per cent). It is used in the treatment of many skin diseases (eczema, impetigo, erysipelas, etc.), and also in the treatment of other skin lesions (burns, bedsores, etc.). Its use by the armed forces in the treatment of burns was authorized at the beginning of the last war, but this action was rescinded in the face of the demonstrated toxicity of boric acid.

#### HYDRIODIC ACID AND HYDROGEN IODIDE

##### *Diluted Hydriodic Acid*, *U. S. P. XIII*

Formula, HI. Molecular Weight, 127.93

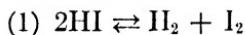
**History and Occurrence.**—Clément and Desormes identified hydrogen iodide in 1813. During the same year it was investigated by

Gay-Lussac. The acid was introduced into medicine by Dr. Buchanan, Junior Surgeon of the Glasgow Infirmary, primarily as a less irritant means of administering iodine. In his own words "It appeared to me, however, that it would be well to save the stomach the labor of preparing hydriodic acid, by giving, for the purposes of medicine, not free iodine, but the hydriodic acid itself."<sup>1</sup> Very small amounts of hydrogen iodide have been found in volcanic gases.

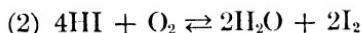
**Physical Properties.**—Hydrogen iodide is a colorless gas having a penetrating odor. It fumes strongly upon exposure to air and is readily liquefied at 0° C. under a pressure of 4 atmospheres. Liquid hydrogen iodide boils at -35.5° C., and has a specific gravity of 2.847 at  $\frac{2}{4}^{\circ}$ . When further cooled, it becomes a solid which melts at -50.9° C. Both gaseous and liquefied hydrogen iodide are non-conductors of electricity. It is exceedingly soluble in water. One volume of H<sub>2</sub>O at 10° C. and 760 mm. pressure dissolves 425 volumes of HI, giving a 70 per cent solution. At 127° C., a 57 per cent solution distils without decomposition.

The U. S. Pharmacopœia XIII Diluted Hydriodic Acid is a colorless or not more than a pale yellow, odorless, aqueous liquid, having a specific gravity of about 1.100 (25° C.). Decomposition of the diluted acid is retarded by the presence of about 0.8 per cent of hypophosphorous acid.

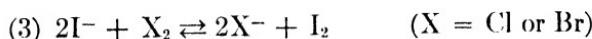
**Chemical Properties.**—Hydrogen iodide (gaseous III) is the least stable of the hydrogen halides, decomposing into H<sub>2</sub> and I<sub>2</sub> at elevated temperatures (1).



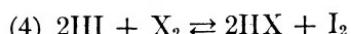
It burns readily with O<sub>2</sub> to liberate I<sub>2</sub> and H<sub>2</sub>O (2).



Hydriodic acid (aqueous solution of HI) behaves in most respects like hydrochloric and hydrobromic acids (*i. e.*, as a strong acid), but is the least stable of the hydrohalide acids. Aqueous solutions are colorless when freshly prepared, but assume a brown color on standing because of the liberation of free iodine (2). Hydriodic acid readily reacts with Cl<sub>2</sub> and Br<sub>2</sub> to liberate I<sub>2</sub> (3) (4).



or written molecularly



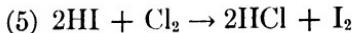
Because hydriodic acid is a powerful reducing agent it has been used for that purpose by organic chemists.

**Tests for Identity.**—1. Aqueous solutions of hydrogen iodide are strongly acid to litmus paper.

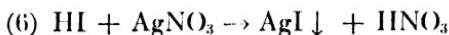
2. Hydriodic acid unites with all metallic oxides and hydroxides (except Cr<sub>2</sub>O<sub>3</sub>) to form iodides.

<sup>1</sup> Am. J. Pharm., 3, 175-6 (1838).

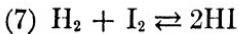
3. When chlorine water is added drop by drop to an aqueous solution of hydrogen iodide or a soluble iodide, the solution is colored yellow to red, due to liberated iodine (5). When this solution is shaken with chloroform, the latter is colored violet. The iodine thus liberated gives a blue color with starch T.S.



4. Silver nitrate test solution produces a yellow, curdy precipitate of silver iodide (6) which is insoluble in nitric acid and in ammonia T.S.

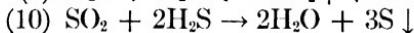
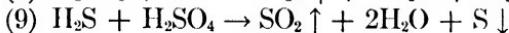
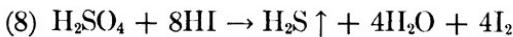


**Commercial Manufacture.**— Hydrogen iodide may be prepared by the direct union of its elements in the presence of a catalyst. This process involves the passing of hydrogen and iodine vapors over heated platinum black (7).

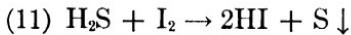


The union takes place slowly and, since the reaction is a decidedly reversible one, always remains incomplete. The product obtained in this manner is impure and unsatisfactory from a medicinal standpoint.

Hydrogen iodide cannot be prepared by the action of sulfuric acid on an iodide because it is very unstable, parting with its hydrogen with ease, and reducing the sulfuric acid. The primary product of the reduction is  $\text{H}_2\text{S}$  (8). As soon as the temperature has been raised sufficiently by the heat of reaction, nearly all of the hydrogen iodide is oxidized. Sulfur is frequently precipitated, due to a secondary reaction between the hydrogen sulfide and the sulfuric acid (9), and between the sulfur dioxide so formed and the excess of hydrogen sulfide present (10).



Hydrogen iodide may be prepared by the action of hydrogen sulfide upon iodine in aqueous suspension (11).

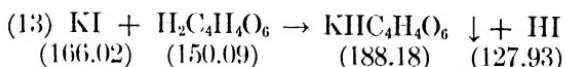


The precipitated sulfur is filtered off and the liquid concentrated to about 57 per cent of HI by distilling off the water.

Hydrogen iodide is usually made by mixing amorphous (red) phosphorus and a large excess of iodine and allowing water to drop slowly upon them (12). The reaction starts easily and the gaseous hydrogen iodide is freed from iodine vapors by passing the gas through a tube containing amorphous phosphorus.

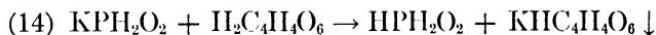


**Laboratory Preparation.**—Dissolve 12.2 Gm. of tartaric acid in 40 cc. of diluted alcohol. Transfer the solution to a bottle of about 100 cc. capacity and add a solution of 13.5 Gm. of potassium iodide in 25 cc. of water and 2 cc. of U. S. P. Hypophosphorous Acid. Shake the mixture thoroughly, and set it aside for two hours in an ice-bath (13). Filter off the crystalline precipitate and wash the bottle and precipitate with several small portions of diluted alcohol until the filtrate weighs 100 Gm. Heat gently on a water-bath until all of the alcohol has evaporated, and then add sufficient distilled water to make the product weigh 100 Gm.

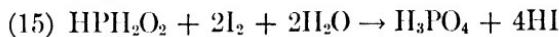


*Note.*—The tartaric acid is dissolved in diluted alcohol (it is more soluble in water) because the alcohol aids in the precipitation of the newly formed potassium bitartrate. The application of cold to the reaction mixture also aids in the precipitation of the potassium bitartrate, since its solubility decreases as the temperature decreases.

If hypophosphorous acid is not available, the correct amount in the finished Acidum Hydriodicum Dilutum may be obtained by dissolving 1 Gm. of potassium hypophosphite with the potassium iodide in the 25 cc. of water and increasing the amount of tartaric acid from 12.2 Gm. to 13.65 Gm. (14).



Hypophosphorous acid is a powerful reducing agent, and hence retards the decomposition of the hydrogen iodide. Also, it may react with any liberated iodine to form phosphoric acid and hydriodic acid (15).



**Pharmaceutical Preparations and Uses.**—1. *Diluted Hydriodic Acid* (Acidum Hydriodicum Dilutum), U. S. P. XIII.—This acid is a solution containing, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of HI, and not less than 0.6 Gm. and not more than 1 Gm. of HPII<sub>2</sub>O<sub>2</sub>. Hydriodic acid is said to produce less stomach disorder than iodides and, like them, is used for the effect of the iodide ion. A discolored (amber to brown) acid or syrup should not be administered, as it may produce severe gastric irritation due to free iodine.

2. *Hydriodic Acid Syrup* (Syrupus Acidi Hydriodici), U. S. P. XIII.—This syrup contains, in each 100 cc., not less than 1.3 Gm. and not more than 1.5 Gm. of HI. It is made by diluting Diluted Hydriodic Acid with distilled water and dissolving sucrose in the liquid by agitation. The product is filtered. The brown color which develops in the syrup on long standing is not necessarily iodine, but may be due to caramelization of the levulose resulting from acid hydrolysis of the sucrose used in the syrup. This syrup

is the most commonly administered form of hydriodic acid, and is much used for its expectorant effect in cough preparations because the iodide ion present stimulates mucous membrane. It is of particular value in liquefying the tenacious sputum which sometimes is associated with bronchitis. Because of the irritant effect of the iodide ion it is not recommended<sup>1</sup> that iodide preparations be used in acute inflammatory conditions of the respiratory mucosa, but rather that it be reserved for the later stages. It should be used only long enough to "loosen" the cough. Average dose—4 cc. (approximately 1 fluidrachm).

## HYDROCHLORIC ACID AND HYDROGEN CHLORIDE

### *Hydrochloric Acid, U. S. P. XIII.*

Formula, HCl. Molecular Weight, 36.47

**History.**—Hydrochloric acid was first obtained by J. R. Glauber in 1648. In 1772, Priestley isolated it in the gaseous condition and thought it was an oxyacid. In 1810, Sir H. Davy showed that it contained only hydrogen and chlorine.

**Occurrence.**—Hydrogen chloride is found in the fumes issuing from active volcanoes in South America and Mexico. When secreted into the stomach, pure human gastric juice contains from 0.4 to 0.5 per cent of free HCl. This appreciable concentration, however, does not usually persist for any length of time, as the acid is neutralized by the saliva, the mucus, and the return flow of the contents of the duodenum to about 0.15 to 0.2 per cent of HCl. The origin of the HCl found in the gastric juice has never been conclusively determined. Whether it arises from the parietal cells in the fundus part of the stomach or whether it is formed by the hydrolysis of a chloride of some weak base, *e. g.*, ammonium chloride, is difficult to say. Hydrochloric acid is necessary to the principal digestive function of the gastric juice, *e. g.*, its action upon protein. In Nature, large quantities of chlorides occur in sea water and in mineral deposits. Sodium chloride is the source of all commercial hydrochloric acid in one way or another.

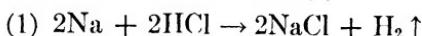
**Physical Properties.**—Hydrogen chloride is a colorless gas having an acrid irritating odor and an acid taste. The density of the gas is 1.2681 (air = 1) and hence it is about 25 per cent heavier than air. One liter weighs 1.6394 Gm. On account of its high critical temperature (52° C.) it can be liquefied by pressure alone. As a liquid (b. p. —5.8° C.) as well as in the gaseous state, it is a non-conductor of electricity. Solid hydrogen chloride melts at —111° C. Its heat of solution is 17,400 (calories per 1 formula-weight of hydrogen chloride in unlimited water).

Hydrogen chloride is very soluble in water. Five hundred and three volumes of the gas dissolve in 1 volume of water at 0° C. (760 mm. pressure) and 460 volumes of the gas dissolve in 1 volume

<sup>1</sup> Goodman and Gilman, *Pharmacological Basis of Therapeutics*, p. 817.

of water at 20° C. (760 mm. pressure). In aqueous solution (18° C.) it is ionized to the extent of 92 per cent in tenth-normal solution and conducts electricity readily. When a saturated solution of hydrogen chloride (43.4 per cent of HCl) is distilled at normal barometric pressure, the gas is driven off until a concentration of 20.24 per cent hydrogen chloride with a constant boiling-point of 110° C. is obtained. Hydrochloric acid of this strength distils unchanged, the water vapor carrying over hydrogen chloride in the same proportion as it exists in the liquid.

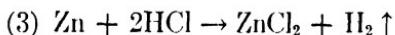
**Chemical Properties.**—Dry hydrogen chloride is quite inactive. It does not react with any of the non-metals (sulfur, phosphorus, etc.). Some of the active metals decompose it, forming hydrogen and the chloride of the metal (1).



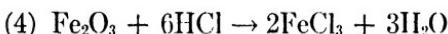
Hydrogen chloride combines directly with ammonia to form ammonium chloride (2).



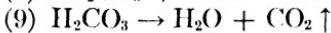
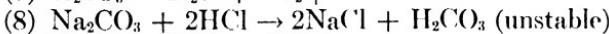
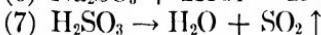
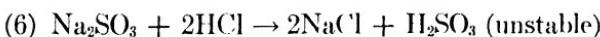
The chemical properties of aqueous solutions of HCl are typical of those of all strong acids. The hydrogen in the acid is displaced by all metals preceding hydrogen in the electromotive series (3).



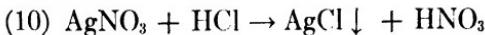
Hydrochloric acid reacts readily with most oxides (4) and hydroxides (5) of the metals to form water and the chloride of the metal.



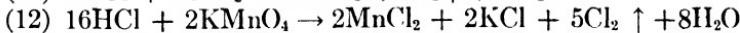
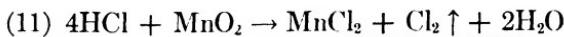
These are known as *neutralization* reactions. The reaction of HCl with sulfites (6) to form SO<sub>2</sub> (7) and with carbonates (8) to form CO<sub>2</sub> (9) is still another type of neutralization reaction.



Because it contains the chloride ion, the acid will precipitate from aqueous solution the water-insoluble chlorides of certain metals, namely Ag, Pb and Hg(ous) (10).



Hydrochloric acid is oxidized by strong oxidizing agents (*e. g.*, KMnO<sub>4</sub>, MnO<sub>2</sub>, etc.), liberating chlorine (11, 12).



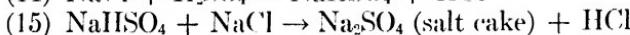
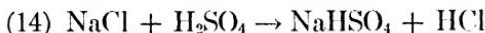
**Tests for Identity.**—1. When Hydrochloric Acid is added to potassium permanganate, chlorine is evolved (12).

2. Hydrochloric acid or its soluble salts precipitate a white, curdy silver chloride from solutions of silver nitrate (10). The precipitate is insoluble in nitric acid. Silver chloride is soluble in ammonia solutions as diammino-silver chloride  $\text{Ag}(\text{NH}_3)_2\text{Cl}$  (13).



**Commercial Manufacture.**—Hydrogen chloride may be made (1) from salt with sulfuric acid, (2) by burning electrolytic chlorine directly in excess hydrogen, and (3) as a by-product in the chlorination of hydrocarbons.

1. The manufacture of hydrochloric acid from salt and sulfuric acid may be depicted as taking place in two steps (14, 15).



Formerly, the salt cake was used in the manufacture of sodium carbonate by the Le Blane Process, but since the advent of the Solvay Ammonia-Soda Process for manufacturing sodium carbonate the use of salt cake has diminished greatly and consequently the production of hydrochloric acid by this method has decreased. The chief use of salt cake today is in the manufacture of glass.

The hydrogen chloride obtained by the first reaction (14) is called "pan acid" and is purer and easier to condense than the "roaster acid" obtained by the second reaction (15). Consequently, the "pan acid" is used principally in the manufacture of the finer grades of hydrochloric acid, whereas the "roaster acid" yields the muriatic acids of commerce. *Muriatic acid* (Latin, *muria*, brine) is a yellow liquid containing a number of impurities, *e. g.*, chlorine, arsenous and sulfurous acids, iron, etc. The color is thought to be due to ferric chloride and yellow organic coloring materials. It contains approximately 35 to 38 per cent HCl. For a more detailed discussion of this method of manufacture, see the third edition of this textbook.

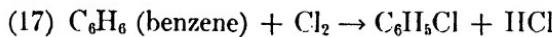
2. A large proportion of the hydrochloric acid manufactured today is made by the burning of electrolytic chlorine in excess hydrogen (16) using quartz bunsen burners, or in some commercial installations hydrogen is burned in an atmosphere of chlorine.



The product is 100 per cent HCl which when dissolved in water in stoneware absorbing systems produces a water-white acid of great purity.

This method has attained prominence because of the extensive manufacture of caustic soda by the electrolytic method in which the by-products are  $\text{H}_2$  and  $\text{Cl}_2$  (see p. 190).

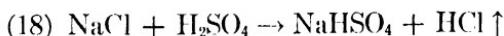
3. Because of the large scale chlorination of hydrocarbons, such as benzene (17) and pentane, considerable quantities of by-product HCl are obtained.



Essentially, for every mole of  $\text{Cl}_2$  used, a mole of HCl is formed. The amount of HCl obtained in this way often becomes a problem to the manufacturer, and cases are on record where the manufacturer pays to have the hydrochloric acid removed from the premises.

**Laboratory Preparation of Dry Hydrogen Chloride.**—Pure, dry hydrogen chloride gas may be prepared by adding U. S. Pharmacopoeia hydrochloric acid to concentrated sulfuric acid in the following manner: A gallon bottle is fitted with a two-hole rubber stopper. A dropping funnel with a long outlet tube is introduced through one hole until the end of the tube reaches to within  $\frac{1}{8}$  inch of the bottom of the bottle. An outlet tube is placed through the other hole in the stopper. About a liter of concentrated sulfuric acid is poured into the bottle and the dropping-funnel filled with U. S. Pharmacopoeia hydrochloric acid. The flow of dry hydrogen chloride gas may be controlled by regulating the amount of hydrochloric acid admitted to the bottle. Sulfuric acid has a great affinity for the water in which the hydrogen chloride is dissolved and, upon coming in contact with it, liberates the hydrogen chloride. The hydrochloric acid must not be run too rapidly into the sulfuric acid lest the heat developed by the reaction causes the hydrogen chloride to be liberated with explosive violence.

**Laboratory Preparation of Hydrochloric Acid.**—Introduce about 30 Gm. of sodium chloride (free from lumps) into an 800 cc. flask, provided with an outlet-tube and dropping-funnel. The outlet-tube is connected in series with two condensing bottles containing distilled water and with a third bottle partially filled with weak sodium hydroxide solution. Slowly run 36 cc. of concentrated sulfuric acid into the flask. A reaction takes place immediately and continues some time without the application of heat (18). When the reaction slows down, gently heat the reaction mixture for one-half hour, then remove the burner, disconnect the bottles and place the flask under a hood.



The hydrogen chloride passes over into the first absorption-bottle where most of it is absorbed by the water. That which escapes passes into the second bottle, where the remainder is held in solution. Any gas coming from the second condensing bottle may be passed through a weak solution of sodium hydroxide. By adding a drop of phenolphthalein to the alkaline solution it is possible to ascertain whether the gas coming from the second absorption bottle is free from hydrogen chloride. Determine whether the product in the condensing vessels responds to all tests for hydrochloric acid. The acid formed by the above procedure is not the official acid, but suffices to illustrate qualitatively the method of preparing it.

**Pharmaceutical Preparations and Medicinal Uses.**—1. *Hydrochloric Acid* (*Acidum Hydrochloricum*), U. S. P. XIII.—Hydrochloric Acid is an aqueous solution containing not less than 35 per cent and not more than 38 per cent of HCl (w/w). It is a colorless,

fuming liquid. The odor and fumes disappear when the acid is diluted with 2 volumes of water. It has a specific gravity of about 1.18 at 25° C.

2. *Diluted Hydrochloric Acid* (*Acidum Hydrochloricum Dilutum*), U. S. P. XIII.—Diluted Hydrochloric Acid is an aqueous solution containing, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of HCl. It is prepared by mixing 234 cc. of Hydrochloric Acid with a sufficient quantity of Distilled Water to make 1000 cc. Diluted Hydrochloric Acid (diluted with 25 to 50 volumes of water) is administered in gastric achlorhydria (lack of hydrochloric acid in the gastric juices). The therapeutic dose usually given is not sufficient to cause the secretion of natural hydrochloric acid in the stomach, but it does appear to give some relief from the achlorhydria. Certain investigators feel that sufficient acid should be administered at each meal to cause the appearance of the free acid in the gastric juices. This necessitates a dose of approximately 10 cc. of the Diluted Hydrochloric Acid in contrast to the usual dose of about 1 or 2 cc. In any event, the acid should be taken in a diluted form through a drinking tube to minimize the danger of its solvent action on the enamel of the teeth. To avoid this difficulty, the preparations such as glutamic acid hydrochloride ( $\text{HOOC}(\text{CH}_2)_2\text{CH}(\text{NH}_2)\text{COOH} \cdot \text{HCl}$ ) and betaine hydrochloride ( $\text{C}_5\text{H}_{11}\text{O}_2\text{N} \cdot \text{HCl}$ ) have been advocated. These compounds are crystalline and may be administered in capsule form. They liberate HCl in the stomach, the glutamic acid residue being metabolized at the same time. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Ipecac Fluidextract* (*Fluidextractum Ipecacuanhæ*), U. S. P. XIII.—Hydrochloric acid is added to this preparation in a 3.5 per cent concentration following extraction of the drug with an alcoholic menstruum to provide a definite acid reaction. This is for the purpose of stabilizing the fluidextract with respect to its alkaloidal content. Average dose—Emetic, 0.5 cc. (approximately 8 minims).

4. *Aconite Fluidextract* (*Fluidextractum Aconiti*), N. F. VIII.—Hydrochloric acid is used in Aconite Fluidextract for the sole purpose of adjusting the pH so that it falls within the range of 2.75 to 3.25. At this pH it has been shown that the fluidextract retains its alkaloidal potency for the longest period of time. It has been used to some extent to slow the pulse and to reduce fever, but with no scientific support. Average dose—0.06 cc. (approximately 1 minim).

5. *Aconite Tincture* (*Tinctura Aconiti*, *Tinctura Aconiti P.I.*), N. F. VIII.—Hydrochloric acid is used in this tincture, as in the fluidextract, for the purpose of adjusting the preparation to a pH of  $3 \pm 0.2$  for stability purposes. Average dose—0.6 cc. (approximately 10 minims).

6. *Arsenious Acid Solution* (*Liquor Acidi Arseniosi*, *Hydrochloric Solution of Arsenic*, *Arsenic Chloride Solution*), N. F. VIII.—Fifty cc. of Diluted Hydrochloric Acid is required to prepare 1000 cc. of Arsenious Acid Solution. The function of the Diluted

Hydrochloric Acid is to convert the arsenic trioxide ( $\text{As}_2\text{O}_3$ ) to arsenic trichloride ( $\text{AsCl}_3$ ), which on dilution with water will hydrolyze at least in part to arsenious acid ( $\text{H}_3\text{AsO}_3$ ). (See p. 512.) Average dose—0.2 cc. (approximately 3 minims).

7. *Compound Cinchona Tincture* (*Tinctura Cinchonæ Composita*), N. F. VIII.—Hydrochloric acid is used in this preparation (1) to facilitate extraction of the alkaloids of cinchona as the water-soluble hydrochlorides as well as (2) to keep them in solution once they have been extracted. The preparation is used principally as a bitter tonic and the presence of the mineral acid makes it of some service in the treatment of atonic dyspepsia. Average dose—4 cc. (approximately 1 fluidrachm).

8. *Ergot Extract* (*Extractum Ergotæ*), N. F. VIII—Hydrochloric acid is used in the extraction of the ergot alkaloids from defatted ergot. The menstruum used is composed of 2 volumes of hydrochloric acid and 98 volumes of diluted alcohol. Ergot and its preparations are used for the powerful stimulating and, therefore, constrictor effect they have on the pregnant uterus. It is also often used in the third stage of labor as a precaution against post-partum hemorrhage. Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains).

9. *Ergot Fluidextract* (*Fluidextractum Ergotæ*, *Extractum secalis cornuti fluidum acidum P. I.*), N. F. VIII.—Hydrochloric acid is used in the menstruum in the same concentration and for the same purpose as in Ergot Extract (*q. v.*), namely, to insure more complete extraction of the alkaloids. The hydrochloric acid remains in this preparation whereas it is removed more or less completely by evaporation in the preparation of the extract. Average dose—2 cc. (approximately 30 minims).

10. *Ipecac Tincture* (*Tinctura Ipecacuanhæ*, *Tinctura Ipecacuanhæ P. I.*), N. F. VIII.—Fifteen cc. of Diluted Hydrochloric Acid is required in the preparation of 1000 cc. of Ipecac Tincture. The hydrochloric acid is used to insure complete solubility of the alkaloids of ipecac, *i. e.*, emetine and cephaeline. Average dose—0.6 cc. (approximately 10 minims).

11. *Nitrohydrochloric Acid* (*Acidum Nitrohydrochloricum*, *Nitromuriatic Acid*, *Aqua Regia*), N. F. VIII.—Nitrohydrochloric Acid is a concentrated aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine. This acid is effective in activating pepsin, and is also believed to stimulate the flow of bile. It is used to some extent in subchlorhydria and in cholangitis. The acid is administered in a well-diluted form, but should be freshly prepared. Average dose—0.2 cc. (approximately 3 minims).

12. *Diluted Nitrohydrochloric Acid* (*Acidum Nitrohydrochloricum Dilutum*, *Diluted Nitromuriatic Acid*), N. F. VIII.—Diluted Nitrohydrochloric Acid is a diluted aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine. It is prepared by diluting 220 cc. of Nitrohydrochloric Acid with sufficient Distilled Water to make 1000 cc. Its use is the same as that of the

more concentrated acid. Average dose—1 cc. (approximately 15 minims).

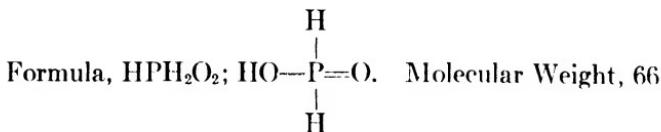
13. *Nux Vomica Tincture* (*Tinctura Nucis Vomicea*, *Tinctura Strychni P. I.*), N. F. VIII.—This tincture contains a small amount (3:75 per cent) of Hydrochloric Acid in the liquid used to macerate the drug prior to percolation. This acid converts the alkaloids to the more soluble alkaloidal hydrochlorides, thus facilitating their extraction. The liquid used for adjusting the alkaloidal content of the finished preparation also contains a small amount of hydrochloric acid. Previous to the use of hydrochloric acid, the acid in common use was acetic acid. It is claimed by some that acetic acid is superior to hydrochloric acid inasmuch as it gives rise to less color in the product than does hydrochloric acid with no loss of alkaloidal potency. Average dose—1 cc. (approximately 15 minims).

14. *Pentobarbital Elixir* (*Elixir Pentobarbitali*), N. F. VIII.—Six cc. of Diluted Hydrochloric Acid are used in this preparation to prepare 1000 cc. of the elixir. The function of the hydrochloric acid is to just exactly neutralize the 4 Gm. of Pentobarbital Sodium also present in the elixir. This gives rise to the free pentobarbital (non-official) together with a small amount of sodium chloride. Average dose—4 cc. (approximately 1 fluidrachm).

15. *Podophyllum Resin* (*Resina Podophylli*, *Podophyllin*), N. F. VIII.—The percolate from the complete percolation of Podophyllum with alcohol is concentrated to a thin syrup and this is poured with stirring into 1000 cc. of water containing 10 cc. of Hydrochloric Acid. The acidulated water is cooled before the precipitation procedure. The acid water is said to give a greater yield of resin than distilled water. Average dose—10 mg. (approximately  $\frac{1}{6}$  grain).

### HYPOPHOSPHOROUS ACID

*Hypophosphorous Acid*, U. S. P. XIII



**History and Occurrence.**—Hypophosphorous acid was discovered in 1816 by Dulong. H. Rose investigated it more thoroughly in 1826. In 1874, Thompson obtained it in crystalline form. It does not occur in Nature. The acid, in the form of its salts, was “introduced by Churchill, 1855, against tuberculosis on the theory that phthisis is caused by lack of oxidation and that this would be stimulated by organic phosphorus; and that the hypophosphites would be converted into this ‘phosphatide element.’ On the basis of this fantastic theory, they were considerably used as tonics in tuberculosis.”<sup>1</sup>

<sup>1</sup> Sollmann: A Manual of Pharmacology, 6th ed., p. 883.

**Physical Properties.**—At ordinary temperatures, pure hypophosphorous acid is a colorless, syrupy liquid having a specific gravity of 1.493 at 18.8° C. At 17.4° C. it becomes a white crystalline solid which melts at 26.5° C. It is soluble in water.

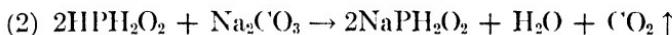
The official hypophosphorous acid is a colorless or slightly yellow, odorless liquid, containing not less than 30 per cent and not more than 32 per cent of  $\text{H}_2\text{P}\text{H}_2\text{O}_2$ . It has a specific gravity of about 1.130 at 25° C.

**Chemical Properties.**—The chemical properties of the acid may be considered as falling chiefly into the following categories: (1) acidic properties, (2) reducing properties and (3) decomposition of the acid.

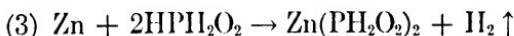
1. The acid acts as a monobasic acid because only one of the three hydrogens present in the formula is ionizable (1).



It may be neutralized with metal hydroxides or carbonates (2) to form the corresponding hypophosphate salt.

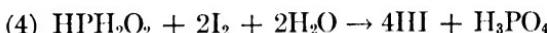


It is a sufficiently strong acid to react with some of the metals, such as zinc (3) and iron, to form hydrogen and the corresponding hypophosphite.



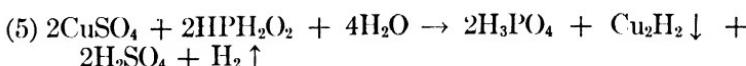
All salts of the acid are soluble in water except ferric hypophosphite.

2. Hypophosphorous acid is readily oxidized to form phosphoric acid and, therefore, acts as a powerful reducing agent. An example of its reducing action as applied to a pharmaceutical preparation has been cited under the discussion of hydriodic acid, in which preparation it acts to reduce any free iodine formed back to the iodide (4).



Because of its reducing property, the acid has been used for the preservation of Ferrous Iodide Syrup, in which capacity it acts to reduce free iodine and ferric ion back to iodide and ferrous ion respectively (see p. 613).

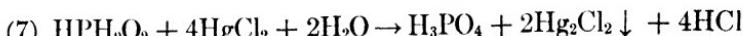
When heated to 60° C. with a solution of  $\text{CuSO}_4$ , a reddish precipitate of impure cuprous hydride ( $\text{Cu}_2\text{H}_2$ ) is formed (5). If the solution is boiled, the hydride decomposes to metallic copper and hydrogen.



Solutions of potassium permanganate are immediately decolorized through reduction with hypophosphorous acid (6).

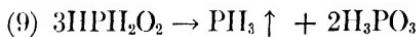


The acid will form a white precipitate with mercuric chloride solutions (7), and in the presence of an excess of the acid the reduction causes the formation of free mercury (8).

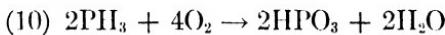


There are many other examples of reduction with hypophosphorous acid, but the above represent most of the important ones. One can readily see from the above reactions that any reducible substance (oxidizing agent) combined with the acid would constitute an incompatibility.

3. When concentrated hypophosphorous acid is heated between 130° and 140° C., it decomposes into phosphorous acid ( $\text{H}_3\text{PO}_3$ ) and hydrogen phosphide (phosphine) (9).



The phosphine is ignited on contact with air (10), because it is associated with the spontaneously inflammable phosphorus dihydride ( $\text{PH}_2$  or  $\text{P}_2\text{H}_4$ ) which forms simultaneously in small amounts. Pure phosphine does not ignite on contact with air.



**Tests for Identity.**—1. It is acid to litmus even in a highly diluted form.

2. It responds to all the tests for hypophosphite ion:

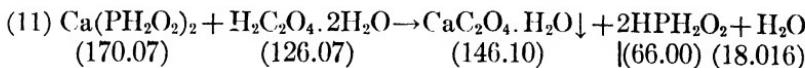
(a) When heated it liberates spontaneously inflammable phosphine (9) (10).

(b) It yields a white precipitate with mercuric chloride T.S. (7). This precipitate becomes gray with an excess of hypophosphorous acid because mercurous salt is easily reduced to free mercury (8).

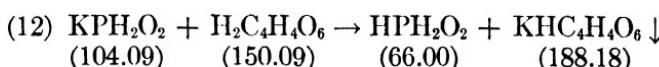
(c) It gives a red precipitate of  $\text{Cu}_2\text{H}_2$  when warmed with copper sulfate T.S. (5).

**Commercial Methods of Manufacture.**—Hypophosphorous acid is made commercially in three ways:

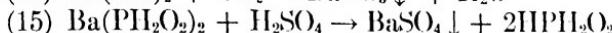
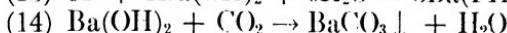
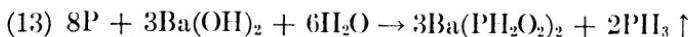
1. By decomposing boiling aqueous solutions of calcium hypophosphate with oxalic acid (11), filtering off the insoluble calcium oxalate and concentrating the acid filtrate in vacuum.



2. By mixing a concentrated aqueous solution of potassium hypophosphate with a hydro-alcoholic solution of tartaric acid (12), allowing the mixture to stand at 5° C. for twenty-four hours, separating the insoluble potassium bitartrate, washing it with diluted alcohol and concentrating the filtrate.



3. By gently heating white phosphorus in an open dish with baryta water until hydrogen phosphide ( $\text{PH}_3$ —very poisonous) ceases to be evolved (13). The excess of barium ion is precipitated by passing in carbon dioxide (14). After filtering, the liquid is evaporated until the barium hypophosphite crystallizes out. This is dissolved in water and decomposed with the theoretical amount of sulfuric acid (15). The mixture is filtered and the filtrate evaporated in an open dish, care being taken not to heat the liquid over  $110^\circ \text{ C}$ . Upon cooling, white crystalline hypophosphorous acid separates out.



The U. S. Pharmacopœia gives appropriate tests for barium, oxalates, heavy metals, and arsenic (from sulfuric acid) because of the above methods of manufacture.

**Laboratory Preparation.**—Dissolve 50 Gm. of calcium hypophosphate in 300 cc. of boiling water. Add a solution of 37 Gm. of oxalic acid in 150 cc. of water and digest the mixture for one hour on a water-bath. Filter off the calcium oxalate and test the filtrate for oxalate ion by adding 1 cc. of calcium chloride test solution to 10 cc. of the filtrate (no turbidity). Concentrate the oxalate-free filtrate on a water-bath to 55 cc. The product should contain about 31 per cent of  $\text{HPII}_2\text{O}_2$  and respond to all the tests for hypophosphorous acid.

**Pharmaceutical Preparations and Uses.**—1. *Hypophosphorous Acid* (Acidum Hypophosphorosum), U. S. P. XIII.—Hypophosphorous Acid should contain not less than 30 per cent and not more than 32 per cent of  $\text{HPII}_2\text{O}_2$ . It is a powerful reducing agent, and hence is used in medicinal preparations to prevent oxidation and resulting decomposition of various ingredients, *e. g.*, hydriodic acid in hydriodic acid syrup, ferrous iodide in ferrous iodide syrup, etc. The acid itself is rarely administered internally, but has enjoyed some popularity in the form of its salts. The use of hypophosphites has been quite conclusively proven to be of little value inasmuch as they pass through the body virtually unchanged. At one time it was thought that compounds of this type would be more easily assimilated by the body, particularly in nerve and brain tissue. This unwarranted assumption has been responsible for their use as nerve tonics.

2. *Diluted Hydriodic Acid* (Acidum Hydriodicum Dilutum), U. S. P. XIII.—(See p. 107.)

3. *Ferrous Iodide Syrup* (Syrupus Ferri Iodidi, Sirupus ferrosi iodidi concentratus P. I.), N. F. VIII.—In addition to other ingredients, Ferrous Iodide Syrup contains 5 cc. of official hypophosphorous acid in each 1000 cc. of the syrup to protect it from oxidation (see p. 613).

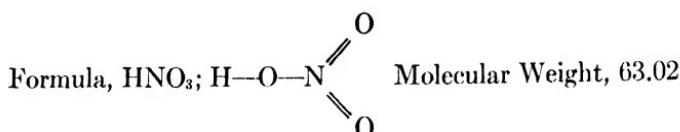
4. *Hydriodic Acid Syrup* (*Syrupus Acidi Hydriodici*), U. S. P. XIII.—(See p. 107.)

5. *Hypophosphites Syrup* (*Syrupus Hypophosphitum*), N. F. VIII.—Hypophosphites Syrup contains, besides other ingredients, 1 cc. of hypophosphorous acid in each 1000 cc. of the syrup. In this syrup it promotes and maintains the solubility of the salts.

6. *Compound Hypophosphites Syrup* (*Syrupus Hypophosphitum Compositus*), N. F. VIII.—In addition to other ingredients, the compound syrup contains 5 cc. of official hypophosphorous acid in each 1000 cc. of syrup for the solubility effects stated above, and also to solubilize the quinine and strychnine alkaloids occurring in the syrup.

### NITRIC ACID AND HYDROGEN NITRATE

*Nitric Acid*, N. F. VIII

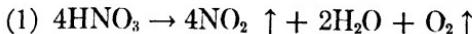


**History and Occurrence.**—Nitric acid is mentioned in the “*Inventione Veritatis*” ascribed to Geber in the eighth century. It was made by calcining a mixture of niter, alum and blue vitriol. Nitric acid was described by Albert le Grand in the thirteenth century, and later by Raimon Lull. The latter obtained it by heating potassium nitrate and clay, and he called the product “*eau forte*” (strong water). The character of nitric acid was not determined until the eighteenth century, when A. L. Lavoisier (1776) proved that it contained oxygen. In 1784 H. Cavendish determined its constitution and showed that it could be made by electrical discharges through moist air. About 1684 Glauber devised the process in use today, *viz.*, the distillation of niter with concentrated sulfuric acid.

This acid exists to a slight extent in some waters, the air (after a thunderstorm) and in the humus of the soil. In combination with sodium, potassium, ammonium, magnesium and calcium, nitric acid occurs widely distributed in Nature. When animal or vegetable matter decomposes, ammonia and other nitrogenous products result. Through the agency of nitrifying bacteria, these products of putrefaction are oxidized to nitric acid, which in turn reacts with the mineral constituents of the soil to form nitrates. These nitrates occur in immense deposits (5 feet thick, 2 miles wide, and 220 miles long) containing from 20 to 60 per cent of sodium nitrate in rainless desert regions of Peru and Chilean Bolivia. Smaller deposits of potassium nitrate, or Bengal saltpeter, occur in Spain, the trans-Caspian region, India, Persia and other oriental countries.

**Physical Properties.**—Hydrogen nitrate (anhydrous  $\text{HNO}_3$ ) is a colorless, mobile, strongly fuming liquid. It has a specific gravity

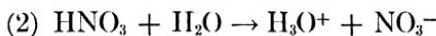
of 1.502 at  $\frac{20}{4}^{\circ}$  and boils at  $86^{\circ}$  C. At this temperature it begins to decompose into water, oxygen and nitrogen dioxide (1).



Hydrogen nitrate may be converted to a solid with a melting-point of  $-42^{\circ}$  C. Concentrated nitric acid forms a constant boiling mixture with water. This mixture boils at  $121.6^{\circ}$  C. ( $251^{\circ}$  F.), contains 68 to 68.5 per cent of nitric acid, and has a specific gravity of 1.41 at  $25^{\circ}$  C. It is exceedingly hygroscopic and corrosive. On mixing nitric acid with water there is a rise in temperature and a contraction in volume. It is miscible in all proportions with water.

**Chemical Properties.**—The chemical properties of nitric acid may conveniently be classified in three groups: (1) acidic properties, (2) oxidizing properties, (3) nitrating properties.

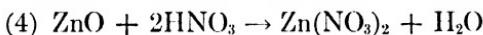
1. Hydrogen nitrate, when dissolved in water, is highly ionized, and is therefore a strong acid (2).



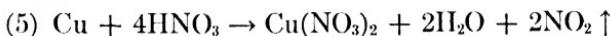
Because of this property it neutralizes bases just as does any other substance capable of forming hydronium ions (3).



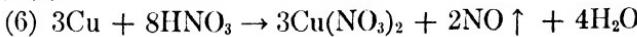
Whenever it can exhibit its property of reacting with a metal oxide to form the nitrate without effecting an oxidation it is again apparent that its activity is that of an acid (4).



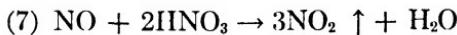
2. Nitric acid acts as an oxidizing agent on both metals and non-metals in many cases, even in *dilute solutions*. It attacks all common metals except gold and platinum under favorable conditions. The manner in which it reacts with metals is greatly influenced by the concentration of the acid, and also by the position of the metal in the electromotive series with respect to hydrogen. For example, when copper (below hydrogen in the electromotive series) is dissolved in *concentrated* nitric acid the main by-product is  $\text{NO}_2$  (5).



However, the *dilute* acid gives as the main by-product nitric oxide ( $\text{NO}$ ) (6).

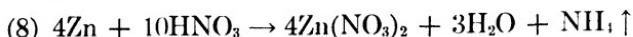


It is not surprising that the above reactions take place because if  $\text{NO}$  did form in the first reaction (5) it would necessarily bubble through concentrated acid on its way out of solution and would very likely be oxidized to  $\text{NO}_2$  (7).

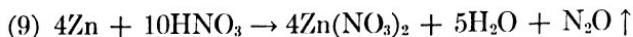


If one adds equation (7) to equation (6) it is readily apparent that equation (5) results.

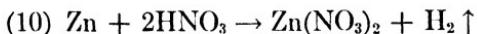
On the other hand, if zinc (above H in the electromotive series) is treated with concentrated acid it yields ammonia (8), which immediately combines to form ammonium nitrate.



The dilute acid with zinc yields principally nitrous oxide ( $\text{N}_2\text{O}$ ) (9).



These reactions may be explained by the fact that hydrogen would be formed by any acid reacting on a metal above hydrogen in the electromotive series (10).

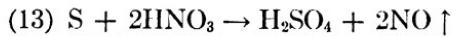


However, this hydrogen is a strong reducing agent and is in contact with nitric acid (a strong oxidizing agent) thus affecting a more or less complete reduction of the nitric acid, yielding in one case  $\text{NH}_3$  (11), and in the other  $\text{N}_2\text{O}$  (12).

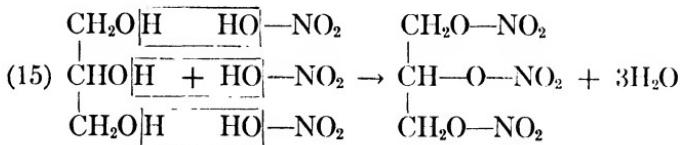


If equation (11) is added to equation (10) the result is equation (8), illustrating the action of concentrated nitric acid on Zn. Likewise, if equation (12) be added to equation (10), the result is equation (9), which expresses the reaction of dilute nitric acid on Zn.

Non-metals are also readily attacked by nitric acid as illustrated by these typical equations (13, 14).



3. Nitric acid is utilized extensively as a nitrating agent for organic compounds, usually in the form of "mixed acid" (nitric acid and sulfuric acid mixed in varying proportions at the acid plant for any specific nitrating job). For example, it is used to nitrate glycerin in the preparation of nitroglycerin (15).



The purpose of the sulfuric acid in "mixed acid" is to bind the water formed in the nitrating reaction, thus preventing dilution of the nitric acid. The group  $-\text{NO}_2$  is a *nitro group*.

**Tests for Identity.**—1. Nitric acid responds to the tests for nitrates.

(a) Mix the diluted nitric acid or solution of a nitrate with an equal volume of concentrated sulfuric acid and allow to cool. Now add a concentrated solution of ferrous sulfate in such a way that the two liquids do not mix. In the presence of nitric acid or a

nitrate, a purple ring, changing to brown, will form at the junction of the two liquids (16, 17).

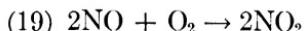


This test is commonly known as the "brown ring" test. The composition of the brown material ( $\text{FeSO}_4 \cdot \text{NO}$ ) is not known with certainty and equation (17), therefore, is not necessarily an accurate representation of what takes place.

(b) Nitric acid gives off brown fumes of  $\text{NO}_2$  when it reacts with silver (18), copper (5), and other metals.



It is to be noted that whenever nitric oxide is formed in a reaction it is readily detected (although colorless) by its easy oxidation to brown  $\text{NO}_2$  (19).



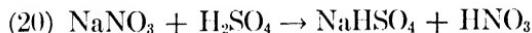
(c) Nitrates do not decolorize acidified potassium permanganate (distinction from nitrites).

2. Nitric acid stains woolen fabrics and animal tissues yellow because substances high in protein, *e. g.*, egg albumen, skin, hair, silk, etc., are acted upon by nitric acid, forming a yellow nitro compound known as *xanthoprotein*.

3. To a solution to be tested add a drop or two of a solution of 1 per cent diphenylamine in concentrated sulfuric acid. A blue color indicates nitric acid or nitrates.

**Commercial Manufacture.**—Nitric acid may be prepared commercially by (1) treatment of Chile saltpeter with sulfuric acid or (2) by the oxidation of ammonia.

1. Until about 1930, a great proportion of nitric acid production was based on this method. At the present time the oxidation of ammonia accounts for almost all of the nitric acid produced. Chile saltpeter ( $\text{NaNO}_3$ ) is treated with sulfuric acid (a non-volatile acid) forming hydrogen nitrate (20).



Although it is possible to cause still further reaction between the sodium hydrogen sulfate and sodium nitrate (21) to produce another mole of hydrogen nitrate it is not customary to do this because it is easier to run off the liquid sodium hydrogen sulfate than to remove a solid sodium sulfate.



The acid sodium sulfate produced is used in the production of other heavy chemicals.

For a more extensive discussion of nitric acid manufacture see previous edition of this textbook.

2. As previously pointed out, approximately 90 per cent of the world production of nitric acid is by the ammonia oxidation process (Fig. 9). The ammonia is prepared on a large scale through the

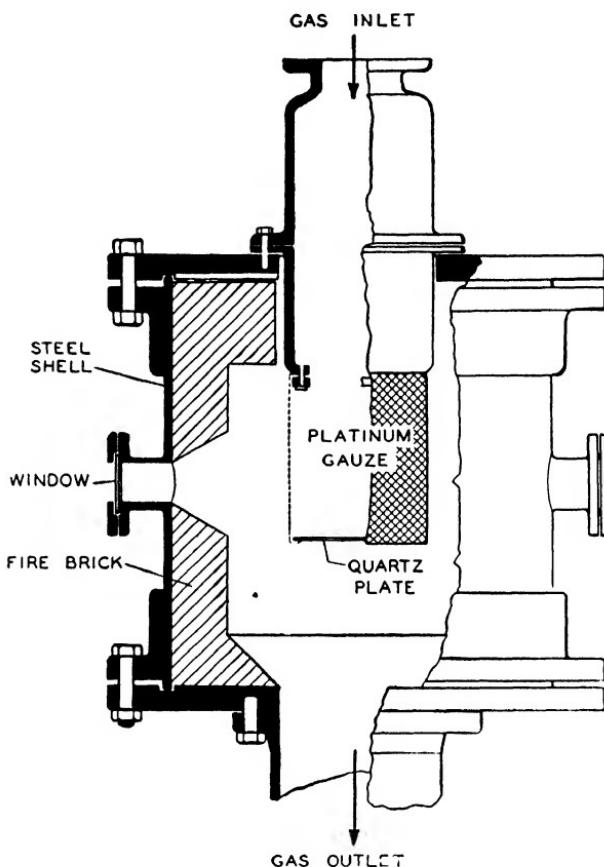
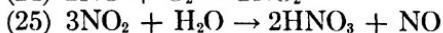
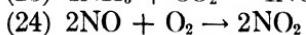
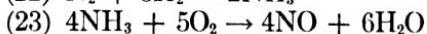
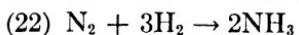


FIG. 9.—Catalyst Chamber for Ammonia Oxidation. (By permission from Badger and Baker, Inorganic Chemical Technology, Copyrighted, 1941, by McGraw-Hill Book Co.)

Haber Process or some modification of it (22). The oxidation of the ammonia is accomplished by the *Ostwald Process*, in which ammonia is mixed with air (21 per cent of O<sub>2</sub>), the mixture heated and rapidly passed through a fine wire gauze of activated platinum raised to a glowing heat. Better than 95 per cent of the ammonia is oxidized to NO, and then to NO<sub>2</sub> (23, 24), which is absorbed by water to form nitric acid (25).



The only disadvantage of this method is that it produces nitric acid of only 50 to 60 per cent concentrations, whereas for many

industrial operations an acid of 98 to 99 per cent concentration is required. However, methods have been devised to concentrate the dilute acid to any specified concentration.

**Laboratory Method of Preparation.**—As previously stated, nitric acid is made by the action of concentrated sulfuric acid upon sodium nitrate (20). This reaction may be illustrated on a small scale by placing 50 Gm. of sodium nitrate in a retort of 300 cc. capacity, and adding 45 Gm. of concentrated acid previously diluted with 13 cc. of water. If necessary, the contents are heated to promote the reaction. Impure nitric acid distills over (contaminated chiefly with  $\text{NO}_2$ ) and should be condensed in a well-cooled receiver. The distillate should respond to all tests for nitric acid.

**Pharmaceutical Preparations and Uses.**—1. *Nitric Acid* (*Acidum Nitricum*), N. F. VIII.—Nitric Acid contains not less than 67 per cent and not more than 71 per cent of  $\text{HNO}_3$ . It has a specific gravity of about 1.41 at 25° C. It boils at 120° C. and is volatilized completely when heated on a steam bath. Nitric acid is used in the manufacture of sulfuric acid (*q. v.*), coal-tar dyes, explosives, nitrates, etc. It is used as an oxidizing agent in the manufacture of pharmaceutical preparations (Ferrie Sulfate Solution, Mercuric Nitrate Ointment, etc.), and externally to destroy chancres, warts, and phagedenic ulcers (rapidly spreading and sloughing ulcers). It is rarely, if ever, prescribed for internal use, although nitric acid is a suitable substitute for hydrochloric acid in gastric achlorhydria.

Nitric acid is a highly corrosive liquid. In contact with the skin, mucous membranes, eyes, gastro-intestinal tract or respiratory mucosa in liquid form (as a spray or splash) or as a vapor, the acid penetrates the tissues, causing destruction proportionate to the concentration of the solution or vapor and the duration of contact. It is imperative that the acid be removed from the skin or other surface by copious flushing with water to prevent damage.<sup>1</sup>

The corrosive properties of nitric acid are not the only dangers, since the gases evolved (nitrous fumes) from spillage on heavy metals or organic materials are also exceedingly toxic. Since the gaseous oxides may cause little or no discomfort *at the time of inhalation*, the victim may proceed about his ordinary work for a few hours until the damage to the lung tissue becomes apparent. Untreated cases frequently terminate fatally as a result of severe pulmonary congestion (edema), *i. e.*, from suffocation.

2. *Bismuth Magma* (*Magma Bismuthi*, Milk of Bismuth, Bismuth Cream), N. F. VIII.—The preparation of 1000 cc. of Bismuth Magma requires 120 cc. of Nitric Acid which is used to convert the bismuth subnitrate to the normal nitrate with sufficient excess acid to prevent hydrolysis of the normal salt. (See p. 548.) Average dose—4 cc. (approximately 1 fluidrachm).

<sup>1</sup> Chemical Safety Data Sheet SD-5, on Nitric Acid, published by Manufacturing Chemists Association of the United States, pp. 12-13, 1946.

3. *Ferric Subsulfate Solution* (Liquor Ferri Subsulfatis, Monsel's Solution, Solution of Basic Ferric Sulfate), N. F. VIII.—Nitric acid is used in the manufacture of this preparation for the purpose of oxidizing the ferrous ion (from ferrous sulfate) to ferric ion. (See p. 632.)

4. *Mercuric Nitrate Ointment* (Unguentum Hydrargyri Nitratis, Citrine Ointment), N. F. VIII.—This ointment is prepared from mercury, nitric acid and lard. (See p. 397.)

5. *Nitrohydrochloric Acid* (Acidum Nitrohydrochloricum, Nitromuriatic Acid, Aqua Regia), N. F. VIII.—This is a strong aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine. (See p. 125.) Average dose—0.2 cc. (approximately 3 minimis).

6. *Diluted Nitrohydrochloric Acid* (Acidum Nitrohydrochloricum Dilutum, Diluted Nitromuriatic Acid), N. F. VIII.—This is a diluted aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine. (See p. 135.) Average dose—1 cc. (approximately 15 minimis).

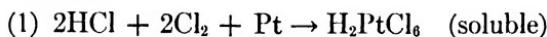
### NITROHYDROCHLORIC ACID

#### *Nitrohydrochloric Acid*, N. F. VIII

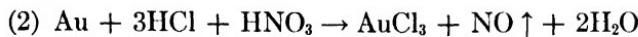
**History and Occurrence.**—Nitrohydrochloric acid does not occur naturally. It was first made by the ancient alchemists who observed its ability to dissolve gold (the king of metals) which was resistant to all other types of acid, hence the name "*aqua regia*" (the kingly water).

**Physical Properties.**—Nitrohydrochloric Acid is a golden yellow, fuming, very corrosive liquid. It has a strong odor of chlorine and an intensely acid reaction to litmus paper, which it afterwards bleaches.

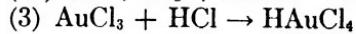
**Chemical Properties.**—This acid is a mixture of hydrochloric acid, nitric acid, nitrosyl chloride ( $\text{NOCl}$ ) and chlorine. Therefore, its chemical properties are those of its components. Because of the chlorine content the acid is a powerful oxidizing agent and it is believed that this accounts for its ability to dissolve gold and platinum (1).



**Tests for Identity.**—The only test given for identity is the requirement that the acid be able to dissolve gold leaf, by converting it to chlorauric acid (2) (2a) (3).

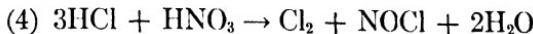


or

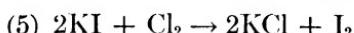


**Commercial Manufacture.**—Nitrohydrochloric Acid, being somewhat unstable, is not marketed as such but should be prepared

fresh when needed. The N. F. directs that 200 cc. of nitric acid (1 mole) be mixed with 800 cc. of hydrochloric acid (3 moles) in a suitable loosely-stoppered container. The mixture is set aside for fifteen hours at room temperature, or until the reaction is complete (4).



Finally the contents are mixed gently to insure uniformity. The mixture should contain sufficient chlorine so that when 1 drop of the acid is added to 1 cc. of an aqueous solution of potassium iodine (1 in 5), iodine will be liberated immediately (5).



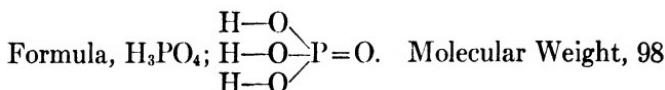
The golden yellow color of the product will fade gradually, in time, yielding a practically colorless solution which is not suitable for use.

**Pharmaceutical Preparations and Uses.**—1. *Nitrohydrochloric Acid* (Acidum Nitrohydrochloricum, Nitromuriatic Acid, Aqua Regia), N. F. VIII.—Nitrohydrochloric Acid is a concentrated aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine. This acid possesses, in general, the same type of activity as hydrochloric acid in treatment of conditions of gastric achlorhydria. It is also said to possess the property of increasing the flow of bile, probably because it relaxes the sphincter muscles of the bile duct, thus permitting the easier flow of bile.<sup>1</sup> A drinking tube should be used for oral consumption. Average dose--0.2 cc. (approximately 5 minims).

2. *Diluted Nitrohydrochloric Acid* (Acidum Nitrohydrochloricum, Diluted Nitromuriatic Acid), N. F. VIII.—This acid is prepared from Nitrohydrochloric Acid (220 cc.) diluted with sufficient distilled water to make 1000 cc. This acid should possess sufficient chlorine to liberate iodine when it is added to an aqueous solution of KI (1 in 5). This acid must be made from Nitrohydrochloric Acid rather than by mixing weaker solutions of nitric acid and hydrochloric acid, since with the weaker acids there is no reaction. Average dose—1 cc. (approximately 15 minims).

## PHOSPHORIC ACID (ORTHO)

### *Phosphoric Acid, N. F. VIII*



**History.**—This principal acid of phosphorus was discovered in 1746 by Andreas Sigismund Marggraf, who observed that this then unknown substance produced peculiar yellow precipitates with silver nitrate and, when calcined with charcoal, yielded elemental phosphorus. In 1833, Thomas Graham published the results of

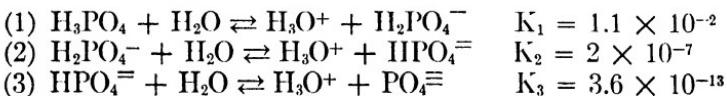
<sup>1</sup> U. S. Dispensatory, 23rd ed., p. 42, 1943.

his masterly investigations of the acids of phosphorus in which he pointed out the differences between the ortho-, pyro-, and meta-phosphoric acids.

**Occurrence.**—Uncombined orthophosphoric acid does not occur in Nature. However, its calcium, aluminum, and iron salts are abundantly found in the minerals *apatite* ( $3\text{Ca}_3[\text{PO}_4]_2 \cdot \text{CaF}_2$ ) and *phosphorite* ( $\text{Ca}_3[\text{PO}_4]_2$ ). The latter is known as "phosphate rock" and occurs as large deposits in Florida, Tennessee, etc. It is the largest source of phosphates for fertilizers. Phosphates occur also in the blood, bone and urine. The slag from steel and iron furnaces contains appreciable quantities of recoverable phosphates. Phosphates are always found in fertile soil and are essential to the development of fruits and seeds.

**Physical Properties.**—When a solution of orthophosphoric acid is evaporated in a vacuum over sulfuric acid, transparent, hard, six-sided, rhombic crystals result. These crystals are very deliquescent in air, have a specific gravity of 1.834 at  $18.2^\circ \text{C}$ . and melt at  $42.3^\circ \text{C}$ . When crystallized from water, the product is a hydrated form,  $2\text{H}_3\text{PO}_4 \cdot \text{H}_2\text{O}$ . Orthophosphoric acid is very soluble in water and in alcohol. The official concentrated solution contains 85 to 88 per cent  $\text{H}_3\text{PO}_4$  and is a colorless and odorless syrupy liquid. Its specific gravity is about 1.71 at  $25^\circ \text{C}$ . Diluted Phosphoric Acid containing from 9.5 to 10.5 Gm. of  $\text{H}_3\text{PO}_4$  in 100 cc. of solution, specific gravity about 1.057, is also official. It is a clear, colorless, and odorless solution.

**Chemical Properties.**—Orthophosphoric acid is a triprotic (tertiary) acid, and consequently ionizes in three steps (1, 2, 3).<sup>1</sup>

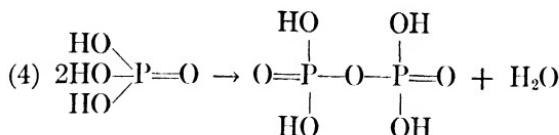


One can see from the ionization constants ( $K_1$ ,  $K_2$ ,  $K_3$ ) that the ionization of the acid takes place in the same manner as any other polyprotic acid, namely each successive ionization step takes place to a lesser extent than the preceding. Actually, the ionization produces very little phosphate ion ( $\text{PO}_4^{=3-}$ ). The acid forms three sodium salts which show very nicely the three possible anions: (1) primary sodium orthophosphate ( $\text{NaH}_2\text{PO}_4$ ), (2) secondary sodium orthophosphate ( $\text{Na}_2\text{HPO}_4$ ), (3) tertiary sodium orthophosphate ( $\text{Na}_3\text{PO}_4$ ). When an aqueous solution of orthophosphoric acid is titrated with sodium hydroxide solution using methyl orange as the indicator the color changes when the salt  $\text{NaH}_2\text{PO}_4$  has formed. When it is titrated using phenolphthalein as the indicator the color changes when the compound  $\text{Na}_2\text{HPO}_4$  has formed. The use of trinitrobenzene as an indicator shows the conversion to  $\text{Na}_3\text{PO}_4$ . In conformity with the results in the titrations, it is

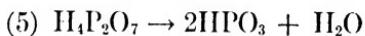
<sup>1</sup> There is a disagreement in most textbooks as to the exact values but, in general and relatively speaking, they agree. These figures are from Handbook of Chemistry (Lange), 5th ed., 1944.

found that when the primary sodium phosphate is dissolved in water it reacts acidic, the secondary phosphate reacts nearly neutral or slightly alkaline, and the tertiary phosphate is exceedingly alkaline.

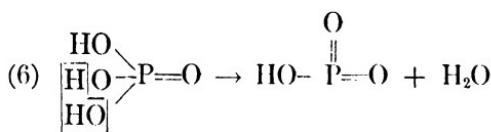
Orthophosphoric acid, when heated to 200° C. loses a mole of water to form pyrophosphoric acid (4) which for purposes of study may be considered to be an *intermolecular* dehydration.



When heated to about 300° C., the pyrophosphoric acid is converted to metaphosphoric acid (5).



However, to simplify the presentation and to fix it more firmly in the student's mind it is convenient to consider that when orthophosphoric acid is heated to 300° C. (neglect the formation of pyrophosphoric acid) an *intramolecular* dehydration takes place (6).



Metaphosphoric acid constitutes the "glacial phosphoric acid" of commerce. It is usually sold in the form of sticks or pellets, the metaphosphoric acid having been hardened by the addition of small amounts of sodium metaphosphate ( $\text{NaPO}_3$ ). Because solutions of this acid slowly change to  $\text{H}_3\text{PO}_4$  (7) they are impossible to keep and, therefore, are no longer officially recognized.

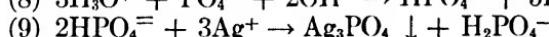
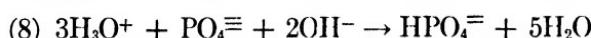


It is of interest to note that phosphoric acid has no oxidizing properties, thus enabling its use wherever a non-oxidizing acid is required (e. g., to prepare HBr from NaBr, where  $\text{H}_2\text{SO}_4$  is unsatisfactory because of its oxidizing action).

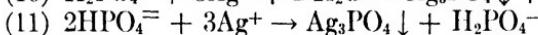
The only water-soluble phosphates are those of the alkali metals and ammonium.

**Official Tests for Identity.**—1. Orthophosphoric acid responds to all general tests for acids.

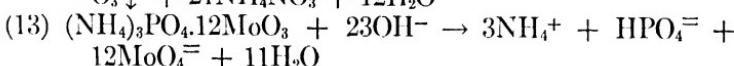
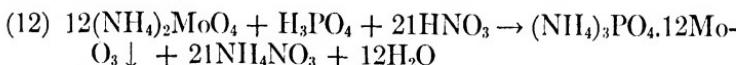
2. When phosphoric acid is carefully neutralized with potassium hydroxide test solution and a solution of silver nitrate added, a characteristic yellow precipitate of silver phosphate results (8 and 9). The precipitate is soluble in ammonium hydroxide and in nitric acid.



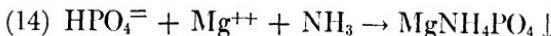
Free orthophosphoric acid forms no precipitate with a solution of silver nitrate. In order to obtain complete precipitation of silver phosphate from solutions of a primary (10) or secondary phosphate (11), the free nitric acid developed in the reaction must be neutralized.



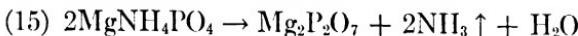
3. Orthophosphoric acid produces a canary yellow colored precipitate when digested at 40° C. with ammonium molybdate solution (nitric acid solution) (12). The precipitate of ammonium phosphomolybdate is insoluble in acids but readily soluble in ammonia water (13).



4. If 3 cc. of the phosphoric acid dilution is rendered alkaline with ammonia water and magnesium sulfate test solution added, a white crystalline precipitate of magnesium ammonium phosphate is produced (14).



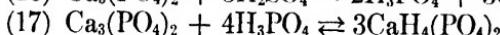
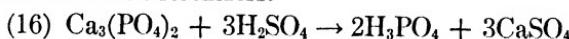
If the dried precipitate of magnesium ammonium phosphate is heated, magnesium pyrophosphate results (15).



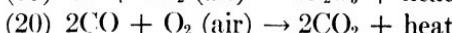
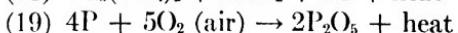
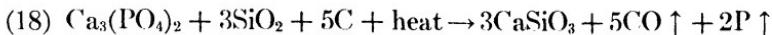
5. When a precipitate of magnesium ammonium phosphate is dissolved in diluted acetic acid and silver nitrate test solution added, a yellow precipitate of silver phosphate is formed (distinction from metaphosphoric or pyrophosphoric acid).

**Commercial Manufacture.**—Orthophosphoric acid is now prepared by (1) the "wet process" and (2) the pyrolytic or thermal methods.

1. Ground phosphate rock or bone ash (principally  $\text{Ca}_3(\text{PO}_4)_2$ ) is treated with sulfuric acid (16) and filtered to remove calcium sulfate and other insoluble materials. The filtrate of dilute phosphoric acid is then concentrated in simple evaporators to about 50 per cent  $\text{H}_3\text{PO}_4$ . Most of the phosphoric acid made by this so-called "wet process" is used in the manufacture of fertilizer, the rest being used for the production of phosphates for industrial use. The acid made by this process is not of food-grade purity unless it is put through a relatively costly purification process. Where ground phosphate rock is treated with "wet process" acid a "superphosphate" of fertilizer grade, containing 40 to 48 per cent of  $\text{P}_2\text{O}_5$  equivalent is produced (17). This is used as a constituent of mixed fertilizers.



2. The greatest advances in phosphoric acid manufacture in the chemical industry have been through the development of the thermal methods. The thermal process consists in smelting phosphate rock with coke and silica at high temperatures (18). A continuous evolution of phosphorus vapor and carbon monoxide issues from the furnace, and they are either burned to produce  $P_2O_5$  (19) and  $CO_2$  (20) or else, more recently, the elemental phosphorus is condensed as such. When  $P_2O_5$  is the product, it is dissolved in water to form phosphoric acid (21).



The principal difference in the thermal methods has been in the type of furnace used.

Until 1939 the *blast* furnace was used extensively to carry out the reduction of phosphate rock, but this process was discontinued in favor of the more efficient *electric* furnaces. For example, in 1937 the Monsanto Chemical Co. began the large-scale production of phosphorus with a very efficient electro-thermal process. Their furnaces are said to be the largest of their kind in the world. Essentially, the reduction of the phosphate rock is carried out in the same manner as previously outlined, but in place of burning the phosphorus that is formed, it is condensed out in a purity of better than 99.9 per cent. The elemental phosphorus is more economical to ship than the phosphoric acid would be. Thus, the phosphorus is shipped to phosphoric acid producing plants to be converted to  $P_2O_5$  and then to acid of exceptional purity. Most of the acid used in chemical manufacturing is prepared by the electric furnace, and is obtainable in the standard concentrations of industrial phosphoric acid, namely, 50, 75 and 85 per cent. Acid of greater strength than 100 per cent is also prepared and is analogous to fuming sulfuric acid.

**Laboratory Preparation.**—Mix 30 Gm. of nitric acid with 30 cc. of distilled water in a glass retort having a capacity of about 200 cc. Having placed the retort on a sand bath, connect it loosely with a well-cooled receiver and add 8 Gm. of yellow phosphorus, previously cut into small pieces under water. Insert a funnel through the opening in the bulb of the retort and carefully apply heat until the reaction begins. If the action is too violent, add a small quantity of water through the funnel. From time to time, return the acid liquid that collects in the receiver to the retort and continue the operation until all of the phosphorus is dissolved or until only insoluble black particles remain, which may be filtered off. If necessary, more nitric acid may be added. Transfer the liquid in the retort to a tared, porcelain evaporating dish and heat on a

sand bath until all of the nitric acid is driven off. The temperature must not exceed 190° C. (p. 127) during the evaporation. Test the products for nitric acid by placing a few drops of the acid in a test-tube with an equal amount of concentrated sulfuric acid. Carefully add a strong solution of ferrous sulfate, so as not to mix the two liquids. No brown ring should appear if the sample is free from nitric acid. Dilute one-half of 1 cc. of the product with 7 cc. of distilled water. Gently warm 5 cc. of this dilution and add 2 cc. of silver nitrate test solution. If the mixture turns brown it indicates the presence of phosphorous or hypophosphorous acid, and the product must be returned to the tubular retort and treated with more nitric acid.

If the product is free from nitric acid and shows no test for phosphorous and hypophosphorous acids, it should be diluted to 100 cc., warmed, and a rapid stream of hydrogen sulfide passed into it for fifteen minutes. The liquid is then set aside for twenty-five hours to allow the arsenic sulfide to precipitate, filtered and concentrated to a syrupy liquid.

**Pharmaceutical Preparations and Uses.**—1. *Phosphoric Acid* (*Acidum Phosphoricum*), N. F. VIII.—Phosphoric Acid should contain not less than 85 per cent and not more than 88 per cent of  $H_3PO_4$ . It is used to a very limited extent (hydrochloric acid is better) in medicine as a tonic and stimulant to the gastric mucous membranes. It aids proteolytic enzymes in the formation of peptones. Phosphoric Acid in a diluted form is used in the treatment of lead poisoning because it lowers the pH of the blood, promoting (1) decalcification of the bones and (2) the associated excretion of lead from the bones at the same time. It is particularly well suited for this type of lead-poisoning treatment (deleading the body) because at the same time that it brings about a beneficial acidosis it also furnishes the lead-solubilizing phosphate ion. In a solution with an acid pH the lead forms the soluble lead phosphate salt rather than remaining as insoluble tertiary lead phosphate.

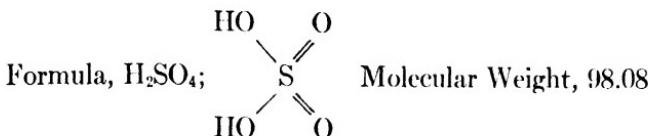
2. *Diluted Phosphoric Acid* (*Acidum Phosphoricum, Dilutum*), N. F. VIII.—Diluted Phosphoric Acid should contain, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of  $H_3PO_4$ . It is prepared by mixing 69 cc. of Phosphoric Acid with sufficient Distilled Water to make 1000 cc. Diluted Phosphoric Acid is given in doses of from 0.1 to 1 cc., largely diluted with water for the purposes discussed under *Phosphoric Acid*. No official dose is given.

3. *Calcium and Sodium Glycerophosphates Elixir* (*Elixir Calcii et Sodii Glycerophosphatum, Glycerophosphates Elixir*), N. F. VIII.—This elixir contains, in addition to other ingredients, 8 cc. of Phosphoric Acid in 1000 cc. of the finished preparation. Average dose—4 cc. (approximately 1 fluidrachm).

4. *Glycerinated Gentian Elixir* (Elixir Gentianæ Glycerinatum), N. F. VIII.—Among numerous other ingredients this preparation contains 5 cc. of Phosphoric Acid in 1000 cc. of the finished elixir.

## SULFURIC ACID AND HYDROGEN SULFATE

### *Sulfuric Acid*, N. F. VIII



**History and Occurrence.**—Sulfuric acid was known to the alchemists in 1440. Basil Valentine prepared an acid, which he called “oil of vitriol,” by heating anhydrous copperas to a high temperature and dissolving the evolved gas in water. Joshua Ward (1685-1761) prepared the same substance by deflagrating a mixture of sodium nitrate and sulfur in large, glass bell jars, absorbing the gases in water and concentrating the solution. Dr. John Roebuck (1718-1794) replaced the glass jars with leaden ones. In 1777, Lavoisier showed that this acid contained sulfur and oxygen, and in 1795 Richter determined its composition. Sulfuric acid in the free state is rarely found in Nature, but it occurs widely distributed in combination with calcium, magnesium, etc.

**Physical Properties.**—Hydrogen sulfate (100 per cent pure) is a colorless, odorless, hygroscopic liquid of oily consistency, having a specific gravity of 1.834 at 15° C. It freezes to a colorless, crystalline mass melting at 10.5° C.

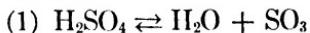
The N. F. VIII describes Sulfuric Acid as a colorless, odorless liquid of oily consistency containing not less than 94 per cent and not more than 98 per cent of  $\text{H}_2\text{SO}_4$ . When strongly heated the acid is vaporized giving off dense, white fumes of  $\text{SO}_3$ . It dissolves in both water and alcohol with the evolution of much heat.

The usual reagent grade of sulfuric acid contains not less than 95.5 per cent  $\text{H}_2\text{SO}_4$  and has a specific gravity of not less than 1.84 at 15.56° C. (60° F.).

Even at the boiling-point of water, sulfuric acid is not volatilized and therefore is classed as a *non-volatile* acid.

**Chemical Properties.**—The chemical properties of sulfuric acid will be considered as follows: (1) stability, (2) hydration, (3) acid properties, (4) oxidizing properties, (5) sulfonating and sulfating properties, and (6) other properties.

1. When heated, pure  $\text{H}_2\text{SO}_4$  is resolved into  $\text{SO}_3$  and  $\text{H}_2\text{O}$  (1). The reaction is reversible.



As the heat is slowly increased, pure  $\text{H}_2\text{SO}_4$  loses increasing amounts of  $\text{SO}_3$  and  $\text{H}_2\text{O}$ , but not in equimolecular amounts (more  $\text{SO}_3$  is

lost than H<sub>2</sub>O). Eventually, at a temperature of 338° C. the H<sub>2</sub>SO<sub>4</sub> distills over constantly, with about 30 per cent of the acid in the dissociated form (1). When the dissociated portion is cooled, it reunites to form a 98.33 per cent solution of H<sub>2</sub>SO<sub>4</sub>. However, when the temperature is increased to 420° C. the dissociation of H<sub>2</sub>SO<sub>4</sub> into SO<sub>3</sub> and H<sub>2</sub>O is practically complete.

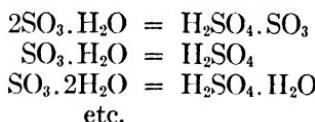
When H<sub>2</sub>SO<sub>4</sub> is suddenly raised to red heat, it is completely decomposed into H<sub>2</sub>O, SO<sub>2</sub> and O<sub>2</sub> (2).



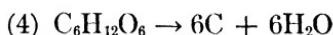
2. Sulfuric acid should *always be added to water* whenever solutions (dilutions) of it are to be made. This precaution should also be observed with other diluents because the amount of heat generated when the two are mixed may cause splashing of the acid. It is believed that the reason for the development of heat is a hydration reaction (3).



The reasons for the above supposition are (1) that a mixture of sulfuric acid and water occupies less volume than would be expected from a simple mixture of two unreacting liquids (in which the volume should be additive), and (2) several compounds of H<sub>2</sub>SO<sub>4</sub> have been isolated, namely H<sub>2</sub>SO<sub>4</sub>.SO<sub>3</sub>, H<sub>2</sub>SO<sub>4</sub>.H<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub>.2H<sub>2</sub>O and H<sub>2</sub>SO<sub>4</sub>.4H<sub>2</sub>O. There is some question as to the manner in which these compounds should be regarded, that is, whether they are hydrates of SO<sub>3</sub> or of H<sub>2</sub>SO<sub>4</sub>. The proponents of the first form infer, for example, that H<sub>2</sub>SO<sub>4</sub> is simply a hydrate of SO<sub>3</sub> (SO<sub>3</sub>.H<sub>2</sub>O). If the hydrates are considered in this manner we have:

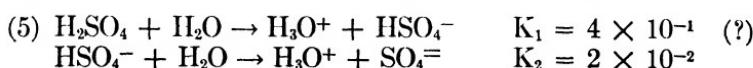


The tendency for sulfuric acid to take up water is so great that it abstracts the elements of water from many compounds containing hydrogen and oxygen. A typical example is the charring of sugar (4).

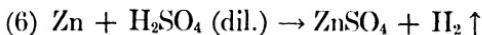


Because of its affinity for water, care should be taken not to leave concentrated sulfuric acid exposed to the atmosphere for long periods of time because there is danger that it will take up enough moisture from the air to even overflow the vessel in which it is stored.

3. Sulfuric acid, particularly in dilute aqueous solutions, behaves as a strong diprotic acid. It ionizes in two steps (5).



It is capable, through the hydronium ion, of dissolving metals *above* hydrogen in the electromotive series with the formation of hydrogen and the sulfate of the metal (6).



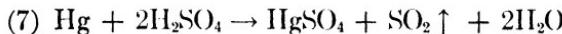
Although the reaction between dilute sulfuric acid and zinc can be construed to be an oxidizing action (zinc to zinc ion  $[\text{Zn} \rightarrow \text{Zn}^{++}]$ ), this is true of all acids (oxidizing and non-oxidizing) because of the hydronium-ion content. The rate of solution in an acid of a metal above hydrogen in the electromotive series is directly dependent upon the hydronium-ion concentration. Sulfuric acid is classed as a "strong" acid although it is not as strong as hydrochloric or nitric acid.

Sulfuric acid will also react in the ordinary manner with metal oxides, hydroxides, carbonates and sulfites (see p. 109).

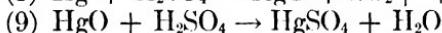
4. *Hot* concentrated solutions of sulfuric acid exhibit an oxidizing action on metals, non-metals and many compounds.

The action on metals *above* hydrogen in the electromotive series has been described.

Metals *below* hydrogen also dissolve in sulfuric acid but sulfur dioxide ( $\text{SO}_2$ ) is liberated instead of hydrogen (7).

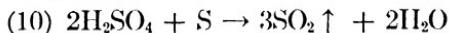


It is believed that the sulfuric acid first oxidizes the metal to the oxide (8) which then reacts with the sulfuric acid to give the sulfate (9).

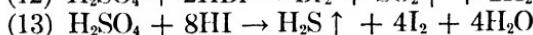
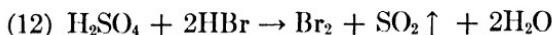


The sum total of equations (8) and (9) is, of course, equation (7).

Non-metals are oxidized more or less readily by sulfuric acid, liberating sulfur dioxide in the process (10, 11).



Among the compounds which are readily oxidized by sulfuric acid are the hydrogen halides (with the exception of  $\text{HCl}$ ). It will be recalled that neither  $\text{HBr}$  nor  $\text{HI}$  could be prepared by the action of sulfuric acid on the corresponding sodium halide because the hydrogen halide formed is readily oxidized. This oxidation takes place at room temperature (12, 13).



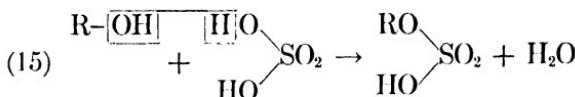
5. Concentrated sulfuric acid is used as a *sulfonating* agent in many organic reactions, because it is capable of replacing a hydrogen attached to carbon (14).



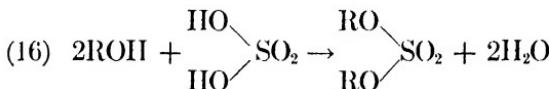
R = aromatic or aliphatic

The process is called *sulfonation* and the product is a *sulfonic acid*. Sulfonations are also carried out with concentrated sulfuric acid to which has been added varying amounts of SO<sub>3</sub>. These fortified acids are known as "oleums" or fuming sulfuric acids.

*Sulfation* is a characteristic reaction of sulfuric acid, forming monoalkyl sulfates and dialkyl sulfates. When the acid is added to an alcohol at room temperature a monoalkyl sulfate is usually formed (15).



The dialkyl sulfates are formed by passing the alcohol and acid vapors over a suitable catalyst (16).



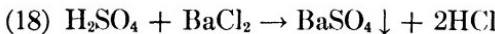
6. As previously stated, sulfur trioxide dissolves in concentrated sulfuric acid to form a somewhat viscous liquid, called "oleum" or fuming sulfuric acid (also Nordhausen acid). Fuming sulfuric acid may contain any specified amount of SO<sub>3</sub>. When cooled, the fuming acid deposits crystals of disulfuric acid (H<sub>2</sub>S<sub>2</sub>O<sub>7</sub>) which are thought to be formed according to the following reaction (17):



Of course, disulfuric acid may also be considered as H<sub>2</sub>SO<sub>4</sub>.SO<sub>3</sub> or H<sub>2</sub>O.2SO<sub>3</sub>.

Sulfuric acid forms two series of salts because of its two replaceable hydrogens. Thus, for example, we have an acid sodium sulfate (NaHSO<sub>4</sub>) and a normal sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>).

**Tests for Identity.**—1. If barium chloride T.S. is added to a dilute solution of sulfuric acid, a white precipitate of barium sulfate (BaSO<sub>4</sub>) is formed (18).



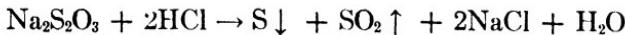
2. If dilute sulfuric acid is treated with lead acetate T.S. a white precipitate forms (19) which is soluble in ammonium acetate T.S.



3. Hydrochloric acid produces no precipitate with sulfates. This distinguishes them from thiosulfates which do give precipitates (20).



but



4. Sulfuric acid chars many organic substances, *e. g.*, wood, sucrose, fibers, etc. As pointed out previously, this is due to

abstraction of the elements of water from the substances leaving a carbon residue (4).

**Commercial Manufacture.**—Sulfuric acid is manufactured by two methods: (1) the *lead chamber process*, and (2) the *contact or catalytic process*. In both processes sulfur (or of lesser importance, iron pyrites) is converted to SO<sub>2</sub> by oxidation. However, the manner in which the SO<sub>2</sub> is converted into sulfuric acid differs greatly in the two processes.

1. The lead chamber process is the older of the two processes, but it has been decreasing in importance from year to year. It derives its name from the fact that the reaction is carried out in large chambers constructed of sheet lead. Lead is not acted on by the concentrations of sulfuric acid obtained in the process. Most of the acid prepared by this process is utilized in the preparation of a fertilizer, superphosphate of calcium.

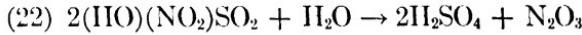
The process is in reality a catalytic process inasmuch as large volumes of sulfur dioxide, oxygen and water are induced to react to form sulfuric acid by a small quantity of nitrous anhydride. There is some doubt as to the exact nature of the reactions taking place in the process but it is thought that the principal reactions taking place are:

A. The conversion of sulfur dioxide into nitrosyl sulfuric acid by means of nitrous acid and oxygen (21).



Nitrosyl sulfuric acid is sometimes written as HNSO<sub>5</sub>.

B. The formation of sulfuric acid and nitrous anhydride by the action of water upon nitrosyl sulfuric acid (22).



C. The anion of nitrous anhydride with water to form nitrous acid (23).



The nitrous acid again combines with any sulfur dioxide that is present to form nitrosyl sulfuric acid according to equation (21).

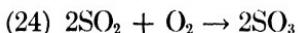
The oxides of nitrogen were formerly obtained from a *nitre pot* which contained sodium nitrate and sulfuric acid, the mixture being heated to obtain the nitric acid vapor. These nitre pots are almost obsolete at the present time because of the use of the catalytic oxidation of ammonia which is a superior process. The SO<sub>2</sub> (together with an excess of oxygen) obtained from the burning of sulfur is passed over the nitre pot or is suitably mixed with the oxides of nitrogen if otherwise produced. The mixed gases are passed into a tower known as a Glover's tower which is packed with quartz. In this tower the gases come in contact with weak acid from the lead chambers and also with more concentrated acid containing dissolved oxides of nitrogen (from the Gay-Lussac tower) which is

known as "Gay-Lussac acid." The hot gases remove the nitrogen oxides from the Gay-Lussac acid and also serve to concentrate the acid flowing downward in the tower. The partially cooled gases then go to the lead chambers, in the first of which most of the sulfuric acid is made. The chambers are large enough to allow sufficient time and space for the reaction to proceed. The acid which forms settles to the floor of the chamber and when enough has formed it can be drawn off and is known as "chamber acid." The exit gases from the chambers are passed into a Gay-Lussac tower which is filled with quartz pieces. The function of this tower is to recover the oxides of nitrogen which have passed through the chambers and which would otherwise be lost. This is accomplished by running the acid (cooled) obtained at the bottom of the Glover tower down the Gay-Lussac tower against the upward rising exit gases from the lead chambers. The gases which finally issue from the Gay-Lussac tower contain only a small percentage of nitrogen oxides and are composed mainly of the nitrogen from the air used in burning the sulfur. For further details about the process, one should consult more detailed works.<sup>1</sup>

The principal drawback to this method of manufacture has been that the acid obtained is at best only 78 per cent H<sub>2</sub>SO<sub>4</sub>, whereas a much more concentrated acid is required for many operations. To obtain a concentrated acid from chamber acid it is necessary to carry out a concentration procedure. This is undesirable in that it increases the cost of the acid.

2. The contact or catalytic process is the most important method for preparing sulfuric acid today. Its great advantage lies in the fact that the process yields sulfuric acid of any desired concentration without the necessity of concentrating the acid. It is especially desirable to have a highly concentrated acid (*i. e.*, contact acid) for nitration procedures.

Essentially, the process depends on the oxidation of sulfur dioxide to sulfur trioxide by the use of a suitable catalyst (24).



The SO<sub>3</sub> which forms can then readily be converted to sulfuric acid.

This process will be better understood by a brief outline of the procedure. Sulfur dioxide is usually obtained by burning sulfur, although some is obtained by roasting iron pyrites. The sulfur dioxide, if prepared from sulfur, requires very little purification, whereas the sulfur dioxide obtained from iron pyrites usually contains many impurities and, to avoid "poisoning" the catalyst, the gas is rigorously purified before being passed into the catalyst. Once the gases have passed through the purification process, they are led into the catalytic converter where they are converted into SO<sub>3</sub> in about a 98 per cent yield. The optimum temperature in the converter is about 450° C. The catalysts used are

Rogers: Textbook of Inorganic Pharmaceutical Chemistry, 3rd ed., p. 135;  
see also Riegel: Industrial Chemistry, 4th ed., p. 15.

of various types. Early contact plants often used platinized asbestos or some other form of platinum catalyst. However, because platinum was expensive, other less expensive metals were sought which would bring about the same conversion. This search led to the discovery of vanadium pentoxide ( $V_2O_5$ ) as a very suitable catalyst. At the present time vanadium catalysts are used more than are platinum catalysts, although recently a highly effective platinized silica gel has been developed. The  $SO_3$  which forms is absorbed in 97 per cent sulfuric acid because the  $SO_3$  gas it obtained in a state which does not combine well with water. However, it does react smoothly with the 3 per cent of water in the 97 per cent acid to form more sulfuric acid (25).



The acid which results is practically 100 per cent pure  $H_2SO_4$  and may be diluted to give a weaker acid or more  $SO_3$  may be passed into it to give the previously discussed "oleums" or fuming sulfuric acids.

**Pharmaceutical Preparations and Uses.**—1. *Sulfuric Acid* (Acidum Sulfuricum), N. F. VIII.—Sulfuric Acid should contain not less than 94 per cent and not more than 98 per cent of  $H_2SO_4$ . The N. F. notes that "*When Sulfuric Acid is mixed with other liquids, it should always be added to the diluent, and great caution should be observed.*"

2. *Diluted Sulfuric Acid* (Acidum Sulfuricum Dilutum), N. F. VIII.—Diluted Sulfuric Acid should contain, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of  $H_2SO_4$ . In a highly diluted form it may be used medicinally in the treatment of achlorhydria since, in common with other inorganic acids, it activates pepsin. It is used little, if any, in present-day medicine.

3. *Ferric Subsulfate Solution* (Liquor Ferri Subsulfatis, Monsel's Solution, Basic Ferric Sulfate Solution), N. F. VIII.—Among other ingredients Ferric Subsulfate Solution contains 55 cc. of Sulfuric Acid as a source of sulfate ion. This solution is used undiluted as a styptic.

4. *Saccharated Ferrous Carbonate* (Ferri Carbonas Saccharatus), N. F. VIII:—Saccharated Ferrous Carbonate requires 3 cc. of diluted sulfuric acid for acidification purposes in the preparation of 1000 Gm. of finished product. (See also p. 629.)

## THE ALKALI METALS

**Introduction.**—The metals comprising this group are lithium, sodium, potassium, rubidium, and cesium. The compounds of the atomic group or radical, ammonium, are discussed after those of potassium to which they show the greatest resemblance.

### Properties of Alkali Metals

Properties	Lithium	Sodium	Potassium	Rubidium	Cesium
Atomic No.	3	11	19	37	55
Atomic weight	6.940	22.997	39.096	85.48	132.91
Isotopes	6, 7	23	39, 40, 41	85, 87	133
Electrons	2 8	2 8 1	2 8 8 1	2 8 18 8 1	2 8 18 18 8 1
Density	0.534	0.971	0.86	1.53	1.87
Melting-point	186°	97.5°	62.3°	38.4°	28.5°
Boiling-point	1336°	880°	760°	700°	670°

The alkali metals are always univalent and their compounds bear a close resemblance to one another. Each member of this family has a relatively low specific gravity, is of a soft waxy consistency, has a low melting-point, and a high metallic luster. With a few exceptions, the salts of the alkali metals are freely soluble in water. The molecules of the alkali metals are considered to be monatomic. These metals form simple cations and never occur as a constituent part of complex anions.

They are the most active and electro-positive of all the metals, the activity increasing as the atomic weight increases. Thus, lithium (atomic weight, 6.94) is the least positive active member of the group (slowly decomposes water), whereas cesium (atomic weight, 132.91) is the most positive active element. All of the alkali metals are oxidized so easily that they must be kept under mineral oil to keep them out of contact with the air. They unite also with hydrogen to form white, crystalline hydrides (MH), which are completely hydrolyzed by water. A common characteristic of the alkali metals is the property of decomposing water violently to form hydrogen and the hydroxides of the respective metals. The latter are highly ionized. Therefore, they are very active bases. The hydroxides of the alkali metals are stable when heated.

## CHAPTER X

### LITHIUM AND LITHIUM COMPOUNDS

#### LITHIUM

Symbol, Li. Valence, 1. Atomic Weight, 6.94; Atomic Number, 3

**History and Occurrence.**—In 1817 J. A. Arfwedson discovered lithium in a silicate known as *petalite*. The free metal was first isolated by Bunsen and Matthiessen in 1855. The name *lithium* (138)

was derived from the Greek word,  $\lambda\thetaos$ , meaning *a stone*, and the element was so named because it was believed to be present only in stones. Also, it was thought that the salts of lithium assisted in dissolving "stones" in the kidneys, gall bladder, etc.

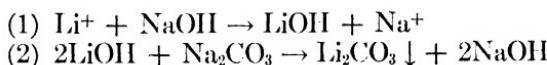
This element does not occur free in Nature. In combination it is found widely diffused. Traces of lithium salts are found in some mineral waters (Mur Springs at Baden-Baden), in soils and in the ashes of many plants, especially in those of tobacco, sugar beet, tea, coffee and sugar cane. It is found in a few minerals, *e. g.*, *spodumene* ( $\text{LiAl}[\text{SiO}_3]_2$ ), *lepidolite* or *lithium mica* ( $\text{KLi}[\text{Al(OH,F)}_2\text{Al}[\text{SiO}_3]$ ), *amblygonite* ( $\text{Li}[\text{AlF}] \text{PO}_4$ ), and *triphylite* ( $\text{Li}[\text{FeMn}] \text{PO}_4$ ). One of the largest sources of spodumene (the most plentiful of the lithium-bearing ores) is the Black Hills of South Dakota.

**Physical Properties.**—Lithium is the lightest of all the metals. It floats easily upon petroleum under which it is preserved. Its density at  $20^\circ \text{ C.}$  is 0.534. It has a silvery-white luster and, though harder than sodium or potassium, it is softer than lead, calcium and strontium. Its toughness permits it to be drawn into wire or rolled into sheets. Lithium melts at  $186^\circ \text{ C.}$  and does not vaporize at red heat. It boils at  $1336^\circ \text{ C.}$  All lithium salts (not the metal) color a flame crimson red and give a characteristic red line together with a less brilliant orange line in the spectrum.

**Chemical Properties.**—Lithium ignites in air at  $200^\circ \text{ C.}$  and burns quietly with a very intense, white light. It decomposes water more slowly than sodium. The metal unites vigorously with oxygen ( $\text{Li}_2\text{O}$ ), hydrogen ( $\text{LiH}$ ), and nitrogen ( $\text{Li}_3\text{N}$ ) to form stable compounds.

**Official Tests for Lithium Ion.**—1. A small quantity of a lithium salt moistened with hydrochloric acid imparts a crimson color to the non-luminous flame of a bunsen burner.

2. Lithium salts in solution, made alkaline with sodium hydroxide, yield with sodium carbonate T.S. a white precipitate on boiling (1) (2).



The  $\text{Li}_2\text{CO}_3$  is soluble in a solution of ammonium chloride.

3. Solutions of lithium salts are not precipitated by diluted sulfuric acid or soluble sulfates (difference from Strontium).

**Commercial Manufacture.**—Lithium may be obtained by electrolyzing (1) fused lithium chloride, (2) a fused mixture of lithium chloride and potassium chloride, or (3) the chloride in solution in pyridine. The very deliquescent lithium chloride is obtained by fusing lithium minerals with barium chloride. The cooled "melt" is lixiviated with water and the resulting solution filtered and evaporated to dryness. The residue is then extracted with a mixture of absolute alcohol and ether, which dissolves the lithium chloride but not the chlorides of sodium and potassium. The alco-

hol-ether mixture is recovered and the residue of lithium chloride thoroughly dried. It is from this fused salt that the metal is obtained by electrolysis. The process is similar to that used for obtaining sodium from sodium chloride (see p. 146).

**Pharmacological Action of Lithium Ion.**—The lithium ion behaves systemically very much like the potassium ion (see p. 225). It is depressant to the nerve centers and to the circulation. The ion has a diuretic action but has no advantages over potassium ion. The lithium ion is somewhat less toxic to the heart than the potassium ion. It stimulates the vagus and a gastro-enteritis is produced by continued administration of even small doses. At one time the great solubility of lithium urate stimulated the use of lithium salts as solvents for uric acid. The reaction between the lithium ion and the urate ion takes place only in concentrations too high to be safely used in the body and, therefore, their employment is irrational.

### LITHIUM BROMIDE

#### *Lithium Bromide, N. F. VIII*

Formula, LiBr. Molecular Weight, 86.86

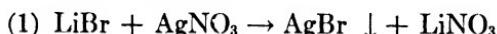
**Physical Properties.**—Lithium Bromide occurs as a white, or pinkish-white granular powder, or in colorless prismatic crystals. It is odorless and has a sharp, slightly bitter taste. Its specific gravity is 3.446 at  $\frac{25}{4}^{\circ}$  and its melting-point  $547^{\circ}\text{C}$ . The salt is so very deliquescent that it goes into solution in its absorbed moisture.

One Gm. of Lithium Bromide is soluble in 0.6 cc. of water at  $25^{\circ}\text{C}$ . and in 0.4 cc. of boiling water. It is freely soluble in alcohol and it dissolves in ether.

At red heat the salt fuses and at higher temperatures it slowly sublimes without decomposition.

**Official Tests for Identity.**—1. A 5 per cent aqueous solution of the salt is neutral or slightly alkaline to litmus paper.

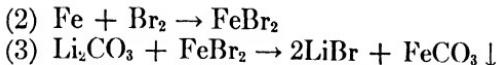
2. Tests for lithium are given under *Lithium Ion* (p. 139).  
3. The addition of silver nitrate test solution to a 5 per cent aqueous solution of the salt produces a yellowish white precipitate of silver bromide, which is insoluble in nitric acid but slightly soluble in ammonia water (1).



4. The addition of chlorine T.S., drop by drop, to a solution of a bromide liberates bromine, which may be dissolved by shaking with chloroform, coloring the chloroform red to reddish-brown.

**Commercial Manufacture.**—Lithium bromide is usually prepared by placing 300 parts of iron wire in a flask, covering it with 900 parts of water, and slowly adding 399 parts of bromine (2). The reaction may be hastened by immersing the flask in warm (not hot) water. When a green solution is obtained, the excess of iron

is filtered off, the filtrate heated, and then agitated with 816 parts of lithium carbonate (3) (*q. v.*). The cooled solution is filtered and evaporated to dryness. Crystals of lithium bromide are obtained by slowly evaporating the highly concentrated solution over sulfuric acid. Approximate yield: 434 parts of lithium bromide.



**Pharmaceutical Preparations and Uses.**—1. *Lithium Bromide* (Lithii Bromidum), N. F. VIII.—Lithium Bromide, when dried at 165° C. for three hours, contains not less than 99 per cent of LiBr. Lithium Bromide and its pharmaceutical preparations are used for the same purpose as potassium bromide. It is more hypnotic than potassium bromide only because of the greater bromide ion content. Average dose—1 Gm. (approximately 15 grains).

2. *Five Bromides Elixir* (Elixir Bromidorum Quinque), N. F. VIII.—The elixir contains, in each 100 cc., the equivalent of not less than 18.5 Gm. and not more than 20 Gm. of Br. Lithium bromide is present to the extent of 3.5 per cent. It is used as a sedative because of the bromide ion. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Bromides Syrup* (Syrupus Bromidorum), N. F. VIII.—This syrup contains, besides other constituents, 8 Gm. of lithium bromide in each 1000 cc. The product, Pentabromides, is similar to this syrup. It is used as a sedative. Average dose—4 cc. (approximately 1 fluidrachm).

## LITHIUM CARBONATE

### *Lithium Carbonate*, N. F. VIII

Formula,  $\text{Li}_2\text{CO}_3$ . Molecular Weight, 73.89

**Physical Properties.**—Lithium Carbonate is a light, white, granular powder, or it occurs in minute monoclinic crystals. Its density is 2.111 at 17.5° C. It is odorless, has an alkaline taste, and is permanent in air.

One Gm. of lithium carbonate is soluble in about 100 cc. of water at 25° C. and in about 140 cc. of boiling water. The solution obtained may not be perfectly clear because of traces of other carbonates or of other allowable insoluble substances. It is almost insoluble in alcohol.

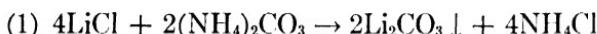
The salt fuses when heated to dull redness and at higher temperatures it loses a part of its carbon dioxide and is partially converted into lithium oxide. The cooled melt consists largely of the pearly oxycarbonate which is permanent in air.

**Official Tests for Identity.**—1. A saturated aqueous solution of lithium carbonate is alkaline to litmus paper and is colored red with phenolphthalein T.S.

2. The salt effervesces when treated with an acid due to the carbonate radical. The evolved carbon dioxide produces a white precipitate when passed through a solution of calcium hydroxide T.S.

3. For lithium tests see lithium ion (p. 139).

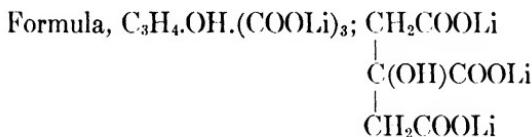
**Commercial Manufacture.**—Lithium carbonate is usually made by boiling a concentrated aqueous solution of lithium chloride, obtained as described on page I39, with ammonium carbonate (1). The precipitate of lithium carbonate is washed with alcohol and dried. In order to save any lithium remaining in solution, the filtrate is evaporated to dryness and the residue of lithium chloride ignited.



**Pharmaceutical Preparations and Uses.**—1. *Lithium Carbonate* (Lithii Carbonas), N. F. VIII.—Lithium Carbonate, when dried at 105° C. for three hours, contains not less than 99 percent  $\text{Li}_2\text{CO}_3$ . Lithium carbonate is used as an antacid (see Sodium Bicarbonate, p. 153), antirheumatic, and diuretic. It is also used to render the secretions slightly alkaline. It is used in the manufacture of some lithia or mineral waters. Average dose ~0.5 Gm. (approximately 7½ grains).

### LITHIUM CITRATE

#### *Lithium Citrate*, N. F. VIII



Molecular Weight, 209.92

**Physical Properties.**—Lithium Citrate occurs as a white powder, or in small white granules. It is odorless and has a cooling, faintly alkaline taste. Upon exposure to moist air, the salt deliquesces and when heated to 165° C. it loses not more than 26 per cent in weight.

One Gm. of Lithium Citrate is soluble in 1.4 cc. of water at 25° C. It is very slightly soluble in alcohol and insoluble in ether.

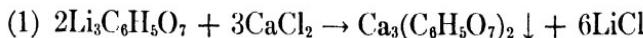
**Chemical Properties.**—When Lithium Citrate is ignited, it decomposes into inflammable vapors having a pungent odor, carbon dioxide, lithium carbonate and particles of carbon. Upon prolonged ignition, a residue of lithium carbonate remains.

**Official Tests for Identity.**—1. A 5 per cent solution of the salt gives a faintly alkaline reaction with litmus paper. The solution is not reddened by 1 drop of phenolphthalein test solution.

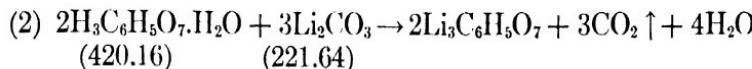
2. Lithium tests given under lithium ion (p. 139).

3. When an aqueous solution of the salt is boiled with an equal volume of calcium chloride test solution there is produced a white

precipitate of calcium citrate (1), which is insoluble in cold potassium hydroxide solution.



**Commercial Manufacture.**—Lithium Citrate is made by adding lithium carbonate to a solution of citric acid until the latter is neutralized (2). The solution is filtered, concentrated, and then allowed to crystallize.



Anhydrous lithium citrate may be obtained by evaporating the solution obtained as above to dryness and heating the residue at 140° C.

**Pharmaceutical Preparation and Uses.**--1. *Lithium Citrate* (Lithii Citras), N. F. VIII.—Lithium Citrate, when dried at 165° C. for three hours, contains not less than 99 per cent of  $\text{C}_3\text{H}_4\text{OH} \cdot (\text{COOLi})_3$ .

Lithium citrate is used for the same purposes as other citrates (see Sodium Citrate, p. 183) and lithium carbonate (*q. v.*). On account of its weak alkaline taste it is more agreeable to take than other lithium salts. Furthermore, it is said to be less irritating to the stomach. Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains).

## CHAPTER XI

### SODIUM AND SODIUM COMPOUNDS

#### SODIUM

Symbol, Na. Valence, I. Atomic Weight, 22.997; Atomic Number 11

**History.**—The metallic element sodium was discovered by Sir H. Davy in 1807 when he electrolyzed sodium hydroxide. Shortly afterward, Gay-Lussac and Thénard suggested a method whereby molten caustic soda could be decomposed by means of red hot iron. This method in turn was succeeded by Brunner's process of igniting sodium carbonate with charcoal. In 1886, Castner recommended the use of sodium hydroxide in place of sodium carbonate and thereby greatly lessened the cost of manufacture. Later, he advocated the use of iron carbide to replace charcoal and this process is still used. In 1890, Castner patented an electrolytic process by which most of the metallic sodium of commerce was made for a long time. In 1924, J. C. Downs patented the process by which metallic sodium is made today.

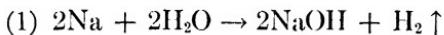
**Occurrence.**—Sodium, like the other chemical elements belonging to the group of alkali metals, is found abundantly and widely distributed in Nature, but always in combination. Sodium chloride forms more than two-thirds of the solids dissolved in sea water. It occurs also in the form of rock salt in the earth. Many compounds of sodium are constituents of spring water, and in combination, sodium is universally distributed in vegetable and animal organisms.

*Soda felspar* ( $\text{NaAlSi}_3\text{O}_8$ ) is present in enormous quantities throughout the rocky crust of the earth. The decomposition of igneous rocks accounts for the presence of sodium compounds in all soils. Sodium carbonate is found widely distributed in Nature as the constituent of many mineral waters and as the principal saline component of natron or trona lakes. Sodium carbonate occurs as efflorescences in lower Egypt, China and Persia, and as a natural deposit in warm and dry districts of many countries, *e. g.*, Egypt, India, and also in California, Nevada and Wyoming. In the latter localities it is usually found mixed with sulfates, chlorides or borates. The crude alkaline crusts of carbonate occurring in Hungary are known as "Szekso." In Nature, sodium sulfate occurs as *thenardite* ( $\text{Na}_2\text{SO}_4$ —anhydrous) in Chile, and in rock salt deposits in Spain. Large deposits of sodium nitrate are found in the district of Atacama and the province of Tarapaca. A double fluoride of sodium and aluminum ( $\text{Na}_3\text{AlF}_6$ ) called *cryolite* is extensively mined in Greenland and elsewhere.

**Physical Properties.**—Sodium is a soft metal having a silvery-white luster when freshly cut. At ordinary temperatures the metal has

the consistency of wax and can be readily cut with a knife. It hardens on cooling. It has a specific gravity of 0.97 (20° C.), a melting-point of 97.5° C., and boils at 880° C., giving a green vapor which is a monatomic gas. Because of its marked tendency to lose an electron and pass from the elemental into the ionic state, sodium occurs fourth in the electromotive series of the metals.

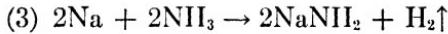
**Chemical Properties of Sodium and Sodium Ion.**—Sodium is very active chemically. Because of this activity it is stored under an inert liquid such as kerosene to retard the action of air and moisture upon it. When exposed to the air, it rapidly becomes covered with a dull gray coating which is a mixture of hydroxide, oxide and carbonate of the metal. When heated in air, it burns with a bright yellow flame, forming sodium monoxide ( $\text{Na}_2\text{O}$ ) and sodium peroxide ( $\text{Na}_2\text{O}_2$ ). Sodium decomposes water with the formation of the hydroxide and the evolution of hydrogen (1), which inflames only when hot water is used.



It also reacts with alcohols in an analogous manner (2).



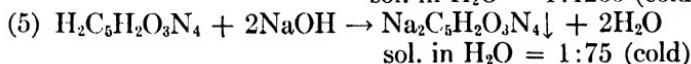
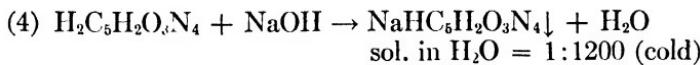
When dry ammonia gas is reacted with sodium metal, a compound known as sodium amide (or sodamide) is formed (3).



The reaction is quite analogous to the reaction of sodium with water.

The element combines directly with most non-metallic elements, especially in the presence of a trace of moisture. Sodium forms an amalgam (an alloy of mercury with another metal), which is said to contain one or more compounds of the two elements, although the amalgam behaves chemically like a simple mixture of the two metals. When the amalgam contains more than a small amount of sodium, it is a solid and is frequently used as an active reducing agent instead of pure sodium because of the ease with which the interactions of the metal with aqueous or alcoholic solutions may be controlled. An amalgam containing 2 per cent of Na is a soft solid having a silvery luster. The reaction of the amalgam may be pictured as simply a reaction of sodium with water or alcohol, since sodium hydroxide (or a sodium alkoxide in the case of an alcohol) together with hydrogen is formed and mercury deposited.

Sodium ion does not form very many insoluble salts, but the few that are known deserve mention. Uric acid, for example, reacts with sodium ion to form two possible salts, the acid urate (4) and the normal urate (5).

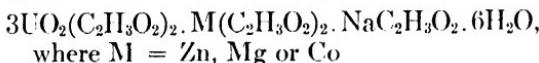


Use has been made of the relative insolubility of the sodium urates together with other chemicals in the chemical demineralization of sea water for the emergency preparation of drinking water.<sup>1</sup>

When a freshly prepared solution of potassium antimonate<sup>2</sup> is added to a neutral or slightly alkaline (with KOH) solution of sodium chloride and the mixture allowed to stand for an hour, a white crystalline precipitate of disodium pyroantimonate (nearly insoluble in water) settles out (6).



There is a group of reagents which forms so-called triple acetates with sodium. Chief among these are zinc uranyl acetate, magnesium uranyl acetate and cobalt uranyl acetate. They have the property of forming relatively insoluble salts with sodium ion having, in general, the following composition:



The zinc salt has been recommended as a reagent for the gravimetric determination of the sodium ion.<sup>3</sup> However, it is said that the cobalt derivative is more suitable for qualitative testing because it is not interfered with by potassium ion.

**Official Tests for Identity of Sodium Ion.**—1. When sodium compounds are converted to the chloride or nitrate salt they will yield a golden-yellow precipitate with cobalt-uranyl acetate T.S. upon agitation. (See under Chemical Properties of Sodium and Sodium Ion.)

2. Sodium compounds will impart an intense yellow color to a non-luminous flame. This test may be said to be almost too sensitive in that it is difficult to tell from the color and intensity of the flame whether significant amounts or mere traces of sodium are present.

**Commercial Manufacture.**—The method of production of metallic sodium has changed in the last twenty years. The most important old or new commercial methods, however, have been electrolytic in nature. The principal difference in the old and new methods is in the electrolyte used.

The older method, now almost obsolete, was the Castner electrolytic process which was used extensively until approximately 1925. Briefly, it depended upon the electrolysis of fused sodium hydroxide (caustic soda) to yield sodium metal and hydrogen at the cathode and oxygen at the anode.

<sup>1</sup> U. S. Patent 2,363,020; see also J. Chem. Ed., **22**, 96 (1945).

<sup>2</sup> Orthoantimonic acid ( $\text{H}_3\text{SbO}_4$ ) is fused with a large excess of potassium hydroxide. The material is then dissolved in water, filtered and evaporated. The hot syrupy solution is digested with a large excess of potassium hydroxide in a silver dish. The alkaline liquid is decanted, granulated and dried in the usual way. This reagent must be kept dry and dissolved only when required for use, because in solution it changes to tetrapotassium pyroantimonate ( $\text{K}_4\text{Sb}_2\text{O}_7$ ), which does not precipitate sodium ion.

\* Barber and Koltoff: J. A. C. S., **50**, 1625, (1928).

In 1924, J. C. Downs patented the electrolytic process now in extensive use. It differs from the Castner process in that the less expensive sodium chloride is used as the electrolyte in place of sodium hydroxide (which must be manufactured from NaCl). Because the melting-point of NaCl ( $804^{\circ}$  C.) approaches the boiling-point of metallic sodium ( $880^{\circ}$  C.) the process at first encountered trouble because it was difficult to collect the sodium metal. High temperatures, such as those existing in the cell, caused the sodium metal to form a "fog" which was exceedingly difficult to condense. However, the addition of electrolytes which are unchanged by electrolysis to the fusion bath was found to bring the melting-point of the bath down to about  $600^{\circ}$  C. and this solved the problem. The Down's Cell is represented diagrammatically in Figure 10.

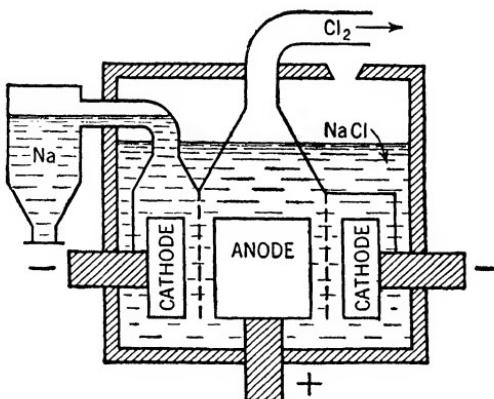


FIG. 10. The Downs Cell. (By permission of Timin, General Chemistry, copyrighted, 1944, by McGraw-Hill Book Co., Inc.)

**Pharmacology of the Sodium Ion.**—The sodium ion is almost devoid of any demonstrable drug or chemical effect upon the human body. This would be expected from the knowledge that sodium ion is normally present in the body fluids in relatively large amounts, and it would be unreasonable to expect pronounced drug effects by adding more sodium ion. However, the sodium ion is extremely important because of the *osmotic* effects it is capable of producing. The sodium ion is the predominant cation in the so-called *extracellular* fluid (that outside the cells, *i. e.*, in the circulation and surrounding the tissue cells), whereas the potassium ion is the predominant cation in the *intracellular* fluid (fluid inside the cells). It is well known that an osmotic gradient (with a consequent flow of water molecules) results when the concentration of water molecules on one side of a semipermeable membrane (permeable to water molecules but not to salts) exceeds the concentration on the other side. Therefore, in the body we have essentially a balanced system of electrolytes where sodium ions (associated with various anions, principally chloride and bicarbonate) exist on one side of a membrane (the cell wall) and potassium ions (also associated with

several anions) exist on the other side. It is believed that it is the sodium ion which is unable to pass through the membrane rather than the potassium ion. In this way, an osmotic gradient is set up in one direction or another through the cell wall, depending on whether the sodium-ion concentration of the extracellular fluid is *hypotonic* or *hypertonic* to the electrolyte concentration of the cell contents (intracellular fluid). If the extracellular solution is hypotonic, water molecules flow into the cell, whereas if the solution is hypertonic water flows out of the cell and it becomes dehydrated. Needless to say, if the sodium-ion concentration is *isotonic* with the cell contents no osmotic gradient exists and, therefore, no flow of water molecules will take place. From the foregoing discussion, it is apparent that while the sodium ion has no specific action on the body tissue, its osmotic function is highly important with regard to the distribution of fluids in the body.

Disturbances causing an abnormal sodium content in the body fluids lead to several well-defined clinical symptoms. Among the common causes for such disturbances may be excessive vomiting, diarrhea or perspiration. A detailed discussion<sup>1</sup> of the alterations in blood sodium and consequent effects is not within the scope of this book. It should be pointed out, however, that the intelligent treatment of conditions arising from abnormal fluid distribution demands a knowledge of the osmotic phenomena bringing about the condition. For example, cardiac patients often display an edematous condition (excess fluid in the tissues). One might jump to the conclusion that since sodium chloride is a diuretic, a good way to get rid of the extra fluid in the tissues would be to administer sodium chloride in sufficient amounts. However, in this case, it would be exactly contraindicated, since it would cause a hypertonic condition of the extracellular fluid. This, of course, would attract water from the intracellular fluid aggravating the edematous condition. For this reason, cardiac patients usually are on a low sodium chloride (or any sodium salt) diet.

#### OFFICIAL COMPOUNDS OF SODIUM

##### SODIUM ACETATE

*Sodium Acetate*, N. F. VIII

Formula,  $\text{CH}_3\text{COONa} \cdot 3\text{H}_2\text{O}$ . Molecular Weight, 136.09

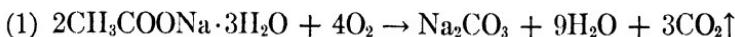
**Physical Properties.**—Sodium Acetate occurs as colorless, transparent monoclinic prisms, or as a granular, crystalline powder. It is odorless or has a faint acetous odor and has a cooling saline taste. When exposed to dry, warm air, the salt effloresces. Its density is 1.45.

<sup>1</sup> Goodman and Gilman: The Pharmacological Basis of Therapeutics, p. 582, 1941.

One Gm. of Sodium Acetate is soluble in about 0.8 cc. of water and in about 19 cc. of alcohol, at 25° C. It is insoluble in ether.

**Official Tests for Identity.**—1. The salt responds to the "Official Tests for Identity of Sodium Ion" (p. 146).

2. When heated to about 58° C., the salt begins to liquefy, and at 120° C. it becomes hard and anhydrous. At higher temperatures it decomposes, emitting inflammable vapors and leaving a residue of sodium carbonate and carbon (1).



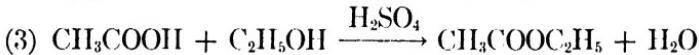
The residue gives positive tests for sodium, is alkaline to litmus paper and effervesces with acids (carbonates).

3. Sodium acetate gives all of the tests characteristic of *Acetates*:

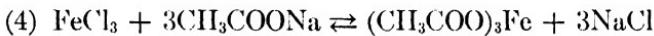
(a) Acidification of sodium acetate or its solutions causes the evolution of an acetic acid (vinegar) odor, particularly if the mixture is warmed (2).



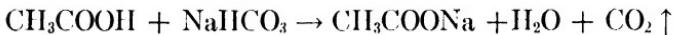
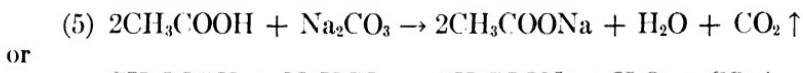
(b) If sodium acetate is warmed with sulfuric acid and ethyl alcohol the acid is esterified to form ethyl acetate which possesses a characteristic odor (3). The acid is formed first according to equation (2), and then the esterification takes place.



(c) Ferric chloride T.S. added to solutions of acetates causes the formation of a deep red color due to ferric acetate (4).<sup>1</sup> This color is destroyed by mineral acids.



**Commercial Manufacture.**—1. Sodium acetate is made by neutralizing acetic acid with sodium carbonate or bicarbonate, filtering, and evaporating the resulting solution to crystallization (5).

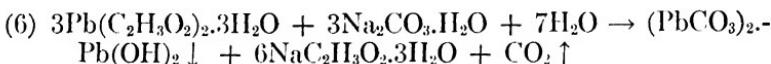


2. It is also made by adding sodium carbonate (in small quantities at a time to avoid too rapid effervescence) to distilled wood vinegar (from pyroligneous acid) until the acid is neutralized. The tarry substances on the surface of the liquid are removed and the brown liquid, after being clarified by standing, is drawn off into shallow iron pans and boiled down to a specific gravity of 1.23. The sodium acetate is then crystallized in sheet-iron boxes. The crystals are drained from the mother liquor and centrifuged. When the impure sodium acetate crystals thus obtained are recrystallized from hot water, a very pure salt is produced. Very often the solu-

<sup>1</sup> Some workers attribute the red color to the formation of colloidal  $\text{Fe(OH)}_3$  from the readily hydrolyzable ferric acetate.

tion of impure sodium acetate is filtered through bone black or boiled with about 10 per cent of the same decolorizing agent. The decolorized solution is filtered, concentrated and crystallized.

**Laboratory Preparation.**—Dissolve 40 Gm. of lead acetate in 120 cc. of water and 13 Gm. of monohydrated sodium carbonate in a like volume of water. Filter each solution and then add the solution of lead acetate to that of the sodium carbonate, stirring briskly.(6). When the precipitate has settled, decant the supernatant liquid, wash the precipitate with a little cold distilled water and add the washings to the decanted liquor. Filter. Then add a sufficient quantity of acetic acid to this solution to render it distinctly acid to litmus paper. Evaporate to 50 cc. and set aside to cool and crystallize. Remove the first crop of crystals and concentrate the mother liquor by evaporation and again allow to crystallize. The product should be dried in a current of air at a temperature not exceeding 30° C.



**Pharmaceutical Preparations and Uses.**—1. *Sodium Acetate* (*Sodii Acetas*), N. F. VIII.—Sodium Acetate, when rendered anhydrous by drying at 120° C., contains not less than 99 per cent of  $\text{CH}_3\text{COONa}$ . The acetate ion itself does not seem to possess any particular therapeutic virtue, except insofar as it is associated with a cation and functions as a means of introducing the cation into the body fluids. Thus, sodium acetate when orally administered is absorbed and easily oxidized in the tissues to sodium bicarbonate. Its physiological action is reflected in the fact that it causes a hypertonic condition of the extracellular fluid which attracts water from the cells into the extracellular fluid. This "salt effect" results in a diuretic action, since the kidneys regulate the electrolyte concentration of the body fluids by excreting water and varying amounts of salts. At the same time the formation of bicarbonate tends to relieve systemic acidosis and lessen the acidity of the urine. Sodium acetate, therefore, is of particular value as a diuretic in the treatment of cystitis and diseases of the urinary tract associated with highly acid urine.

In order to fuse sodium acetate it requires about four times as much heat as is absorbed by an equal volume of water and, because this heat is very slowly evolved, the fused salt is used as a filler for foot warmers and many other types of thermophores. Average dose—1.5 Gm. (approximately 22 grains).

2. *Theobromine and Sodium Acetate* (*Theobromina et Sodii Acetas*), U. S. P. XIII.—"A hydrated mixture of theobromine sodium ( $\text{C}_7\text{H}_7\text{N}_4\text{O}_2\text{Na}$ ) and sodium acetate ( $\text{NaC}_2\text{H}_3\text{O}_2$ ) in approximately molecular proportions. It yields not less than 55 per cent and not more than 65 per cent of theobromine ( $\text{C}_7\text{H}_8\text{N}_4\text{O}_2$ )."  
The purpose of the sodium acetate in this preparation is to solubilize the theobromine by forming a water-soluble double salt. Theo-

bromine preparations are effective diuretics which are of particular value in cardiac edemas. Average dose—0.5 Gm. (approximately 7½ grains).

3. *Theobromine and Sodium Acetate Capsules* (*Capsulae Theobrominae et Sodii Acetatis*), U. S. P. XIII.—These capsules “contain an amount of theobromine,  $C_7H_8N_4O_2$ , equivalent to not less than 53 per cent and not more than 67 per cent of the labeled amount of theobromine and sodium acetate, including all tolerances.”

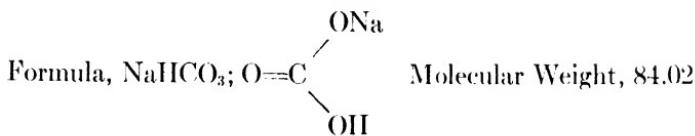
4. *Theophylline and Sodium Acetate* (*Theophyllina et Sodii Acetas*, *Theophylline With Sodium Acetate*), U. S. P. XIII.—“A hydrated mixture of theophylline sodium ( $C_7H_8N_4O_2Na$ ) and sodium acetate ( $NaC_2H_3O_2$ ) in approximately molecular proportion. It yields not less than 55 per cent and not more than 65 per cent of anhydrous theophylline ( $C_7H_8N_4O_2$ ).” This is another double salt of sodium acetate in which sodium acetate acts merely to solubilize the therapeutically effective compound. Theophylline is said to be a better diuretic than theobromine but, because its action is not as lasting and because it exhibits some undesirable side effects, theobromine is the preferred drug. Average dose—0.2 Gm. (approximately 3 grains).

5. *Theophylline and Sodium Acetate Tablets* (*Tabellæ Theophyllinae et Sodii Acetatis*), U. S. P. XIII.—These tablets “contain an amount of anhydrous theophylline ( $C_7H_8N_4O_2$ ) corresponding to not less than 53 per cent and not more than 67 per cent of the labeled amount of theophylline and sodium acetate, including all tolerances.”

#### DISODIUM HYDROGEN ORTHOARSENATE.—(See p. 525.)

#### SODIUM BICARBONATE

##### *Sodium Bicarbonate*, U. S. P. XIII



**Physical Properties.**—Sodium Bicarbonate is a white, odorless, crystalline (monoclinic) powder. It is stable in dry air, but in moist air it slowly decomposes into sodium carbonate, carbon dioxide and water. It has a specific gravity of 2.206.

One Gm. of Sodium Bicarbonate is soluble in 10 cc. of water at 25° C. It is insoluble in alcohol.

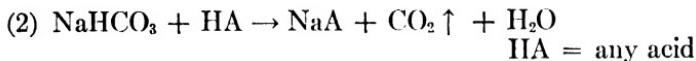
**Chemical Properties.**—When heated, the salt loses water and carbon dioxide and is converted into the normal carbonate (1).



The above decomposition takes place whether the dry salt or a solution of it is heated. It accounts for one of the major difficulties

in attempting to sterilize either the dry salt or solutions of it since the sodium carbonate solution which remains is much more alkaline than the bicarbonate solution and consequently would be dangerous to use parenterally.

Another characteristic reaction of bicarbonate (also carbonates) is that carbon dioxide is liberated when treated with acids (2).



The liberated  $\text{CO}_2$  bubbling through the liquid is called *effervescence*. Effervescent tablets and salts make use of the reaction of sodium bicarbonate with acids (usually organic acids, *e. g.*, tartaric acid, citric acid, etc.), because in the dry state the bicarbonate and acid do not react, whereas, when introduced into water a vigorous evolution of  $\text{CO}_2$  takes place.

A discussion of the chemistry of sodium bicarbonate in a book dealing with its medical aspects would not be complete without mentioning the sodium bicarbonate:carbonic acid buffer system of the blood plasma. The normal acid-base balance of the plasma is maintained by three mechanisms working together: the buffers of the body fluids and red blood cells; the pulmonary excretion of excess carbon dioxide; and the renal excretion of either acid or base, whichever is in excess.

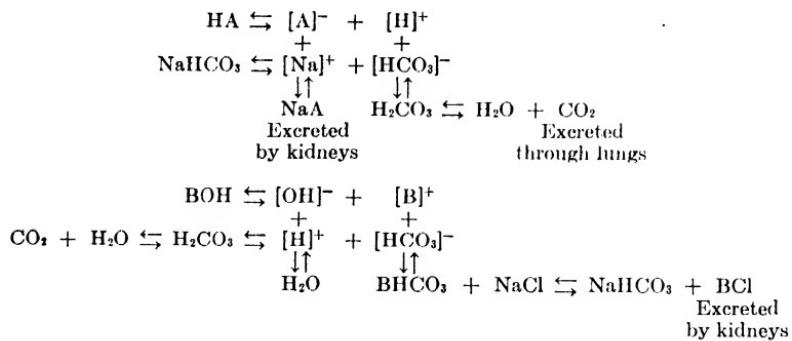
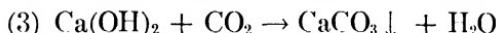


FIG. 11.—Mechanism of bicarbonate: carbonic acid buffer system. "A" represents a radical of fixed (non-metabolizable) acid; "B," a radical of fixed base.

Although there are other buffer systems in the plasma, *e. g.*, (1) the sodium phosphate:sodium biphosphate system (see p. 207) and (2) the proteins, the  $\text{NaHCO}_3:\text{H}_2\text{CO}_3$  buffer system is by far the most important. This buffer system involves an equilibrium between sodium bicarbonate and carbonic acid. At a given pH, the ratio of the concentrations of the two substances is constant. While the workings of the system are complex in detail, they are simple in principle. If an excess of *acid* is liberated in the body, it is neutralized by some of the sodium bicarbonate; the excess carbonic acid decomposes into water and carbon dioxide and the latter is excreted by the lungs until the normal ratio is achieved.

If an excess of *alkali* arises in the body, it combines with carbonic acid to form bicarbonate, and more carbonic acid is formed from carbon dioxide and water to restore the balance. Since carbon dioxide is an end-product of the metabolism of all types of food-stuff, there is always an abundant supply upon which to draw. The situation may be represented as in Figure 11.<sup>1</sup>

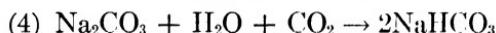
**Official Tests for Identity.**—1. The salt effervesces when treated with acids (2), and the CO<sub>2</sub> which is formed will cause a precipitation of CaCO<sub>3</sub> when passed into lime water (contains Ca(OH)<sub>2</sub>) (3).



2. A cold aqueous solution of sodium bicarbonate, if pure, will not cause phenolphthalein to color red which serves to distinguish it from soluble carbonates. Sodium carbonate, for example, colors phenolphthalein an intense red.

3. An aqueous solution responds to all the tests for sodium ion (*q. v.*).

**Commercial Manufacture.**—Sodium bicarbonate is made by the Solvay Ammonia Soda process which will be described in some detail under Sodium Carbonate (p. 170). It can also be made by passing carbon dioxide into a very cold, saturated aqueous solution of sodium carbonate. On account of its lower solubility in water, sodium bicarbonate precipitates (4).



**Pharmaceutical Preparations and Uses.**—1. *Sodium Bicarbonate* (Sodii Bicarbonas, Baking Soda), U. S. P. XIII.—Sodium Bicarbonate, when dried over sulfuric acid for six hours, contains not less than 99 per cent of NaHCO<sub>3</sub>. Sodium bicarbonate is used medicinally principally for its acid neutralizing properties. It is used (a) to combat gastric hyperacidity, (b) to combat systemic acidosis and (c) for miscellaneous uses.

(a) Because sodium bicarbonate is such a common household chemical it is considered by the layman as a rather innocuous chemical and, in this way, has become quite popular for treating gastric hyperacidity and a multitude of other stomach ailments. It is common for the patient to attempt to treat "gas on the stomach" with sodium bicarbonate or an antacid powder containing it. Since the stomach is normally acid and thus reacts with carbonates or bicarbonates to liberate gaseous carbon dioxide, it is difficult to see where any benefit can be derived.

Of more serious consequence than the occasional use for gastric upset is its continued use in relatively large doses for the mitigation of the pains associated with peptic ulcer. The cause of the peptic ulcer is often traced back to the initial use of sodium bicarbonate, because sufficiently large doses of sodium bicarbonate will effectively neutralize all of the stomach acid and perhaps impart a slightly

<sup>1</sup> Abstracted in part from an article, Alkalosis, Physicians Bulletin, p. 19, published January-February, 1947, by Eli Lilly & Co.

alkaline reaction to the gastric fluids. Since the stomach normally operates at an acid pH this obviously is an abnormal condition. Therefore, when the sodium bicarbonate has been eliminated, the stomach again secretes acid, but usually in larger amounts than were previously found in the stomach. This constitutes what is commonly known as "rebound acidity," and relief from the excess acidity is sought by again using sodium bicarbonate. In this way, a vicious cycle may be set up which can end in the formation of a peptic ulcer.

In spite of the misuses of sodium bicarbonate cited above, the drug is of established value in treating gastric hyperacidity, when used in controlled doses.

Oral administration of the drug also causes a lessening of the acidity of the urine or may even produce an alkalinization. This effect is of value during the administration of certain drugs to increase their effectiveness or lessen the possibility of their crystallizing in the kidneys or urinary tract. Notable among these drugs is sulfanilamide and its related drugs which are often prescribed with sodium bicarbonate for the purpose of preventing if possible the deposition of crystals of the conjugated sulfa drug in the kidney with consequent mechanical injury to that organ.<sup>1</sup> It might be pointed out, however, that the trend of opinion seems to be that large amounts of fluids ingested during the sulfa treatment are more apt to prevent this so-called "crystalluria" than is sodium bicarbonate. More recently, the administration of two or more sulfa drugs simultaneously has been quite effective, based on the principle that a given volume of liquid will hold more of the two (or more) than of any one. In addition to the use of sodium bicarbonate with drugs, it has been shown that changing the reaction of the urine alternately from acid to alkaline may have a beneficial effect in the treatment of certain types of urinary tract infections.

Occasionally, it is found that the simultaneous administration of sodium bicarbonate with other drugs inhibits the activity of the administered drug. Such a therapeutic incompatibility is found in the case of sodium bicarbonate and sodium salicylate<sup>2</sup> which are often prescribed in equivalent amounts, the sodium bicarbonate being administered to alleviate the gastric discomfort attendant upon oral sodium salicylate administration. The investigators found that the administration of sodium bicarbonate and sodium salicylate simultaneously in equal amounts greatly retarded the rise in the serum salicylate level in contrast to sodium salicylate alone which rather quickly brings up the salicylate level. Furthermore, if a satisfactory salicylate level in the blood is reached by sodium salicylate alone, it was found that oral administration of sodium bicarbonate would markedly reduce the level.

(b) Sodium bicarbonate is administered parenterally and orally to combat systemic acidosis. Its effect is mainly to increase the alkali reserve of the blood and to replace sodium ion in cases of

<sup>1</sup> Flippin and Reinhold: *Ann. Int. Med.*, **25**, 433 (1946)

<sup>2</sup> J. A. M. A., **125**, 1173 (1944)

clinical dehydration. Because it could easily be given in excessive amounts causing an alkalosis its intelligent use requires that the alkali reserve of the blood be determined before its administration. Inasmuch as it requires a laboratory analysis to determine the alkali reserve of the blood and because it is so difficult to sterilize sodium bicarbonate, several other sodium salts have been suggested as replacements, *e. g.*, sodium lactate, sodium citrate, etc. These salts are claimed to be superior because the organic portion of the molecule is oxidized in the tissues to yield essentially sodium bicarbonate with the advantage that they can be sterilized and do not tend to cause alkalosis.

(c) When moistened with water, sodium bicarbonate is used as a local application for burns, insect bites, etc. It is also commonly used as a dentifrice although its taste does not lend itself to this purpose very well. Average dose—2 Gm. (approximately 30 grains).

2. *Chinioson* (*Chiniosonum*), U. S. P. XIII.—This preparation contains 7-iodo-8-hydroxyquinoline-5-sulfonic acid, its sodium salt and sodium bicarbonate (about 20 per cent). It is required to contain not less than 26.5 per cent and not more than 29 per cent of iodine (I). The sodium bicarbonate appears in the method of preparation in which 1 part of sodium bicarbonate is added to 4 parts of the sulfonic acid. The reason for the presence in this preparation of three species of compounds is explained on the basis that in the mixing of dry sodium bicarbonate with dry 7-iodo-8-hydroxyquinoline-5-sulfonic acid there is a small amount of moisture unavoidably present which causes a small portion of the ingredients to react. Rather than set up specific requirements for the three components the U. S. P. simply states their presence in the monograph. However, when dissolved in water, the powder effervesces due to the reaction between the acid and bicarbonate and the sodium salt forms. It is used in the treatment of intestinal amebiasis. Average dose—1 Gm. (approximately 15 grains).

3. *Compound Effervescent Powders* (*Pulveres Effervescentes Compositi*, *Seidlitz Powders*), U. S. P. XIII.—These powders come in the form of *blue* papers and *white* papers. “The mixture in a blue paper weighs not less than 9.5 Gm. and not more than 10.5 Gm., and contains not less than 23 per cent and not more than 27 per cent of  $\text{NaHCO}_3$ , and not less than 73 per cent and not more than 78 per cent of  $\text{KNaC}_4\text{H}_4\text{O}_6 \cdot 4\text{H}_2\text{O}$  (potassium sodium tartrate). The white paper contains not less than 2 Gm. and not more than 2.4 Gm. of  $\text{H}_2\text{C}_4\text{H}_4\text{O}_6$  (tartaric acid).” These powders are used as a mild laxative, the effect being principally due to the potassium sodium tartrate. The reaction between the sodium bicarbonate and the tartaric acid produces an effervescence of  $\text{CO}_2$  which adds to the general palatability of the powders. The slight excess of acid imparts a pleasant acidulous taste to the preparation. Average dose—“The contents of a white and of a blue paper, each dissolved in about 60 cc. (2 fluidounces of water), the solutions mixed, and administered just after effervescence begins to subside.”

4. *Phenolsulfonphthalein Injection* (*Injectio Phenolsulfonphthaleini*), U. S. P. XIII.—This preparation contains among other ingredients, 1.43 Gm. of  $\text{NaHCO}_3$  per 1000 cc. This may be replaced by 17 cc. of normal  $\text{NaOH}$  if desired. The sodium bicarbonate (which changes to sodium carbonate when heated) is used in this preparation to convert the water-insoluble phenolsulfonphthalein (Phenol Red) into the water-soluble sodium salt. Sodium hydroxide accomplishes the same purpose. This preparation is used as a diagnostic aid in the estimation of renal (kidney) function by intravenous or intramuscular injection. Normal kidneys excrete the drug readily, whereas in cases of impaired renal function the excretion is slowed up. Average dose of phenolsulfonphthalein—diagnostic—intravenous or intramuscular, 6 mg. (approximately  $\frac{1}{10}$  grain).

5. *Effervescent Potassium Citrate* (*Potassii Citras Effervescens*), U. S. P. XIII.—Effervescent Potassium Citrate contains 47.7 per cent sodium bicarbonate, 20 per cent of potassium citrate, 25.2 per cent of tartaric acid and 16.2 per cent of unefloresced citric acid. The amount of sodium bicarbonate is just sufficient to react with all of the acid present to bring about effervescence due to liberation of  $\text{CO}_2$ . Here again its main function is to improve the palatability of the preparation by acting as a source of  $\text{CO}_2$ . Average dose—4 Gm. (approximately 60 grains). For discussion of uses see Potassium Citrate (p. 243).

6. *Effervescent Sodium Phosphate* (*Sodii Phosphas Effervescens*), U. S. P. XIII.—This preparation is analogous to the foregoing Effervescent Potassium Citrate except that 20 per cent of excised sodium phosphate ( $\text{Na}_2\text{HPO}_4$ ) is used in place of potassium citrate. It is used as a saline laxative and cathartic (see p. 208). Average dose—10 Gm. (approximately  $2\frac{1}{2}$  drachms).

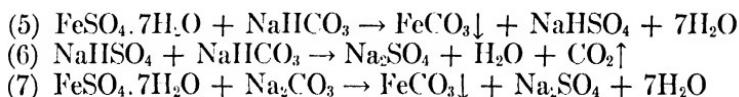
7. *Compound Acetanilid Powder* (*Pulvis Acetanilidi Compositus*), N. F. VIII.—This preparation contains 20 per cent of sodium bicarbonate. The sodium bicarbonate functions as an antacid. Average dose—0.3 Gm. (approximately 5 grains).

8. *Arsenic and Mercuric Iodides Solution* (*Liquor Arseni et Hydriargyri Iodidorum*, *Donovan's Solution*), N. F. VIII.—It requires 9 Gm. of sodium bicarbonate for the preparation of 1000 cc. of the finished solution. The reason for the use of sodium bicarbonate is to reduce the acidity of the solution to approximately pH 6.5 to 7.5. At this pH the stability of the preparation is greatly increased.<sup>1</sup> (For further discussion see p. 406.) Average dose—0.1 cc. (approximately  $1\frac{1}{2}$  minimis).

9. *Cataria and Fennel Elixir* (*Elixir Catariae et Foeniculi*, Catnip and Fennel Elixir), N. F. VIII.—Together with other ingredients this preparation contains 1.8 per cent of sodium bicarbonate. This preparation is used for its carminative and antacid properties, the sodium bicarbonate acting as the antacid. Average dose—for infants: 0.5 cc. (approximately 8 minimis).

<sup>1</sup> Husa: J. A. Ph. A., 21, 211 (1932).

10. *Saccharated Ferrous Carbonate* (Ferri Carbonas Saccharatus), N. F. VIII.—This preparation requires 350 Gm. of sodium bicarbonate for the preparation of 1000 Gm. of Saccharated Ferrous Carbonate. The function of the sodium bicarbonate is to react with the ferrous sulfate to form ferrous carbonate. The bicarbonate is used in preference to sodium carbonate because the reaction of the former (5, 6) liberates carbon dioxide (which retards oxidation of the formed  $\text{FeCO}_3$ ) in contrast to the latter which does not (7). (See also p. 629.)



The preparation is used as a hematinic. Average dose—0.25 Gm. (approximately 4 grains).

11. *Mild Mercurous Chloride and Sodium Bicarbonate Tablets* (Tabellæ Hydrargyri Chloridi Mitis et Sodii Bicarbonatis, Calomel and Soda Tablets), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of HgCl for tablets containing more than 15 mg., and not less than 90 per cent and not more than 110 per cent for tablets containing 15 mg. or less of HgCl." (See p. 415 for a more extended discussion.) Average dose—60 mg. (approximately 1 grain) of Mild Mercurous Chloride, in tablets usually containing a fraction of the average dose.

12. *Rhubarb and Soda Mixture* (Mistura Rhei et Sodæ), N. F. VIII.—This preparation contains 3.5 per cent of sodium bicarbonate in the finished product. The sodium bicarbonate is supposed to overcome the astringent action (by neutralizing tannic acid) and to disguise the taste of the rhubarb. The preparation is used as a cathartic and is said to be of some value for children. Average dose—4 cc. (approximately 1 fluidrachm).

13. *Soda and Mint Solution* (Liquor Sodæ et Menthae, Mistura Sodæ et Menthae, Soda Mint), N. F. VIII.—Contains 50 Gm. of sodium bicarbonate together with 20 cc. of Aromatic Ammonia Spirit dissolved in enough spearmint water to make 1000 cc. of finished preparation. It is clarified by the use of talc, if necessary. The preparation is used as a carminative and antacid preparation. Average dose—8 cc. (approximately 2 fluidrachms).

14. *Sodium Bicarbonate and Calcium Carbonate Powder* (Pulvis Sodii Bicarbonatis et Calcii Carbonatis, Sippy Powder No. 1), N. F. VIII.—The powder contains 77 per cent of sodium bicarbonate and 23 per cent of calcium carbonate. This is one of the powders developed by Dr. Sippy for the treatment of peptic ulcer on the theory that healing could be induced by placing the patient on a bland diet together with continuous ingestion of a mixture of antacid powders. The reduction in stomach acidity then would inhibit digestion and acid corrosion of the ulcer. The administration of the antacid powders in the quantities advocated by Sippy

entails the possibility of incurring systemic alkalosis which can terminate fatally unless corrective measures are taken. However, the success of continuous suppression of the hydrogen-ion concentration of the stomach in peptic ulcer therapy has led to the discovery and development of safer and perhaps more effective chemicals. (See Magnesium Trisilicate, Aluminum Hydroxide, etc.) Average dose—2.6 Gm. (approximately 40 grains).

15. *Sodium Bicarbonate and Calcium Carbonate Tablets* (*Tabellæ Sodii Bicarbonatis et Calcii Carbonatis*, Sippy Powder Tablets No. 1), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{NaHCO}_3$  and  $\text{CaCO}_3$ ." These are simply tablets of Sippy Powder No. 1 in a convenient form for administration.

16. *Sodium Bicarbonate and Magnesium Oxide Powder* (*Pulvis Sodii Bicarbonatis et Magnesii Oxidi*, Sippy Powder No. 2), N. F. VIII.—This powder "contains not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{NaHCO}_3$ , and not less than 90 per cent and not more than 110 per cent of the labeled amount of  $\text{MgO}$ ." The formula used to prepare it requires a fifty-fifty mixture of the two chemicals. It is used as an antacid as described under the discussion of Sippy Powder No. 1. Average dose—1.3 Gm. (approximately 20 grains).

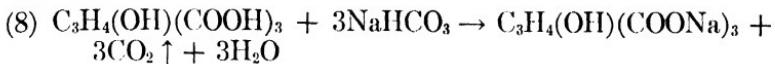
17. *Sodium Bicarbonate and Magnesium Oxide Tablets* (*Tabellæ Sodii Bicarbonatis et Magnesii Oxidi*, Sippy Powder Tablets No. 2), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{NaHCO}_3$ " and not less than 90 per cent and not more than 110 per cent of the labeled amount of  $\text{MgO}$ . Again, the tablets are a convenient form in which to administer Sippy Powder No. 2.

18. *Sodium Bicarbonate Tablets* (*Tabellæ Sodii Bicarbonatis*), N. F. VIII.—These tablets contain "not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{NaHCO}_3$ ." A convenient form in which to administer sodium bicarbonate. The tablets are usually marketed in 5 and 10 grain sizes. Average dose—same as for Sodium Bicarbonate.

19. *Compound Sodium Borate Solution* (*Liquor Sodii Boratis Compositus*, Dobell's Solution), N. F. VIII.—To prepare 1000 cc. of this solution requires 15 Gm. of sodium bicarbonate. Glycerin and liquefied phenol are added to an aqueous solution of sodium borate and sodium bicarbonate, and the mixture allowed to stand half an hour or until effervescence ceases. The product is made up to volume and filtered. (See also p. 164.) For use on mucous membranes—undiluted; or for the dental spray bottle, diluted with 5 volumes of water.

20. *Sodium Citrate Solution* (*Liquor Sodii Citratis*, *Mistura Sodii Citratis*, *Potio Riverii*), N. F. VIII.—This solution is prepared by dissolving sodium bicarbonate in a solution of citric acid contained

in a strong bottle (8). As soon as solution is effected the bottle is stoppered.

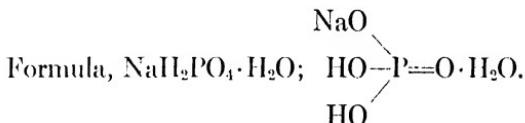


Sodium Citrate Solution is used as a diaphoretic. (See p. 185.) Average dose—15 cc. (approximately 4 fluidrachms).

21. *Diluted Sodium Hypochlorite Solution* (*Liquor Sodii Hypochloritis Dilutus*, Modified Dakin's Solution, *Liquor Soda Chlorinatæ Chirurgicalis*), N. F. VIII.—This solution requires the use of sodium bicarbonate to reduce the alkalinity of the solution to such a point that it will not cause a red coloration with powdered phenolphthalein. For a discussion of the mechanism whereby this takes place, see p. 195. It is used as a disinfectant and irrigant for wounds.

### SODIUM BIPHOSPHATE

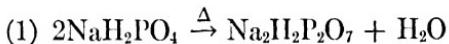
*Sodium Biphasphate*, U. S. P. XIII



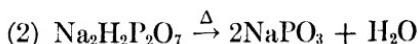
Molecular Weight, 138.01

**Physical Properties.**—Sodium Biphasphate occurs in the form of a white, crystalline powder or as colorless, transparent rhombic prisms. It is odorless and has an acid, saline taste. The salt is slightly deliquescent. It crystallizes in the rhombic system with 1 molecule of water, which it loses at 100° C., and becomes anhydrous. Sodium Biphasphate is very soluble in both cold and hot water, but is practically insoluble in alcohol, in chloroform, and in ether.

**Chemical Properties.**—When the salt is heated to 240° C., it is converted into disodium dihydrogen pyrophosphate (1).

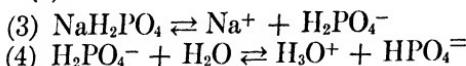


When this salt ( $\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$ ) is heated to 240° C., it is changed into sodium metaphosphate (2) and modifications of sodium metaphosphate, such as  $\text{Na}_2\text{P}_2\text{O}_6$ , etc., the composition of the latter depending upon the conditions of heating.



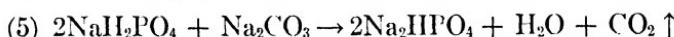
Although sodium biphasphate is a sodium salt of phosphoric acid, it is the result of replacing only one of the hydrogens of orthophosphoric acid with sodium and consequently exhibits acidic properties. The acidic properties can be largely attributed to the ionization of

$\text{H}_2\text{PO}_4^-$  (4) which results from the ionization of sodium biphosphate (3).



The ionization in equation (4) takes place to approximately the same extent as the ionization of hypochlorous acid ( $\text{HOCl}$ ) or the ionization of the first hydrogen in carbonic acid. It is sufficiently acid to decolorize phenolphthalein but is not acidic enough to turn methyl orange yellow. Of course, the  $\text{HPO}_4^{2-}$  is also capable of ionizing but only to such a small extent that it is virtually negligible. (See p. 126.)

**Official Tests for Identity.**—1. Solutions of Sodium Biphosphate are acid to litmus paper and effervesce with sodium carbonate (5).



2. A 1 in 20 solution of sodium biphosphate responds to all of the official tests for sodium ion (*q. v.*) and for phosphate ion (*q. v.*).

**Commercial Manufacture.**—When orthophosphoric acid is added to a solution of secondary sodium orthophosphate and the solution evaporated, monohydrated sodium dihydrogen orthophosphate crystallizes out in rhombic prisms (6).



**Pharmaceutical Preparations and Uses.**—1. *Sodium Biphosphate* (Sodii Biphosphas, Sodium Dihydrogen Phosphate, Monosodium Orthophosphate, Sodium Acid Phosphate), U. S. P. XIII.—Sodium Biphosphate, when dried to constant weight at  $100^\circ \text{ C}.$ , should contain not less than 98 per cent of  $\text{NaH}_2\text{PO}_4$ . This salt is administered internally to produce distinctly acid urine. It renders the urine acid because when absorbed it tends to disrupt the buffer system of phosphates in the blood. However, the kidneys excrete the excess phosphate as sodium acid phosphate which accounts for the urine acidity. The sodium biphosphate may be alternated with sodium bicarbonate for the purpose cited under Sodium Bicarbonate (p. 154), *i. e.*, to cause change of urine reaction from acid to alkaline or *vice versa*. Another important reason for the acidification of the urine is to "activate" certain antiseptic drugs, particularly methenamine. Methenamine itself is not antiseptic, but formaldehyde is liberated from it in acidic media. Formaldehyde, of course, is highly antiseptic and thus the methenamine combined with an acid urine acts as an antiseptic in the treatment of cystitis and other urinary tract infections.

Technical grades are used in some baking powders. Average dose—0.6 Gm. (approximately 10 grains).

2. *Methenamine and Sodium Biphosphate Tablets* (Tabellæ Methenaminæ et Sodii Biphosphatis, Tablets of Methenamine and Acid Sodium Phosphate), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled

amounts of  $(\text{CH}_2)_6\text{N}_4$  and of  $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$ " and are a convenient way of administering sodium biphenylate with methenamine. However, the best way to administer the sodium biphenylate is midway between doses of methenamine.

## SODIUM BORATE

### *Sodium Borate, U. S. P. XIII*

Formula,  $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ . Molecular Weight, 381.43

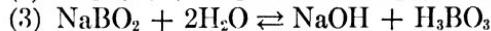
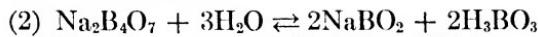
**Physical Properties.**—Sodium borate occurs as colorless, odorless, transparent, monoclinic crystals. It has a sweetish, alkaline taste, and effloresces in warm, dry air. Its specific gravity is 1.694 ( $17^\circ \text{ C.}$ ).

One Gm. of sodium borate is soluble in 16 cc. of water and in about 1 cc. of glycerin, at  $25^\circ \text{ C.}$  One Gm. dissolves in about 1 cc. of boiling water. It is insoluble in alcohol.

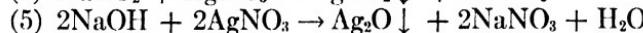
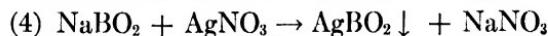
**Chemical Properties.**—When sodium borate is heated, it loses part of its water of hydration and swells to a white, porous product. When the heat is increased to redness, the remainder of the water is expelled and the salt fuses to a colorless liquid, which on cooling forms a transparent mass known as *borax glass* or *bead*. If the formula for sodium tetraborate is written  $(\text{NaBO}_2)_2 \cdot \text{B}_2\text{O}_3$  it will be noted that a considerable excess of boric anhydride ( $\text{B}_2\text{O}_3$ ) is present. This may unite with basic oxides to form mixed metaborates (1). These usually have a characteristic color and are used in qualitative analysis to test for various cations.



An aqueous solution of sodium borate is distinctly alkaline to litmus paper and to phenolphthalein T.S. This is accounted for by the fact that sodium tetraborate is hydrolyzed by water into sodium metaborate and boric acid (2), and the former is further hydrolyzed to sodium hydroxide and boric acid (3). Dilution increases the hydrolysis.



That the hydrolysis takes place as described above can be demonstrated by adding silver nitrate T.S. to a saturated solution of borax. White silver metaborate is precipitated (4). On the other hand, when silver nitrate T.S. is added to a *very dilute* solution of borax, silver oxide (black) is precipitated (5).



When acidified, aqueous solutions of sodium tetraborate will deposit crystals of boric acid (6).



**Official Tests for Identity.**—1. Turmeric paper is colored reddish-brown by an acidulated (HCl) aqueous solution of sodium tetraborate. If the dried paper is moistened with ammonia T.S. the color changes to greenish-black. This is a general test for borates.

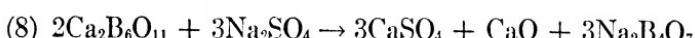
2. When the salt is treated with sulfuric acid, methanol added, and the mixture ignited, it burns with a green-bordered flame. This is a general test for borates, and depends first upon the formation of boric acid according to equation (6), followed by the esterification of the boric acid with the methanol (7) to form trimethylborate which burns with a green flame.



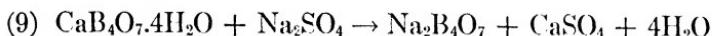
**Commercial Manufacture.**—Ninety per cent of the world supply of borax is said to be manufactured by two American companies.<sup>1</sup>

One of the companies uses the brine obtained from Searles Lake, which is a deposit of various salts with brine filling in the spaces between the crystals. The brine is pumped to the plant and concentrated to obtain deposits of the various chemicals. Potassium chloride is the first salt obtained. Since the mother liquor from it is nearly saturated with borax, cooling of the solution in a vacuum crystallizer yields crude borax. The crude borax, when recrystallized, constitutes commercial borax.

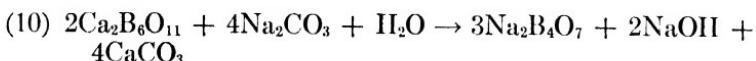
The other company has been working mainly with borax minerals. Until recently, this firm used *colemanite* ( $\text{Ca}_2\text{B}_6\text{O}_{11} \cdot 5\text{H}_2\text{O}$ ) as its raw material. This mineral occurs in immense deposits in California (Death Valley). According to a U. S. patent by Bayley,<sup>2</sup> the mineral is mixed with sodium sulfate and heated to redness (8), but not to fusion, in a rotary furnace. After the mass has cooled, the borax is dissolved in water and allowed to crystallize.



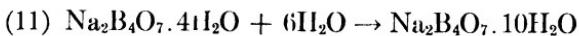
The mineral *borocalcite*,  $\text{CaB}_4\text{O}_7 \cdot 4\text{H}_2\text{O}$ , is also converted into borax by this method (9).



The action of sodium carbonate upon colemanite forms borax, sodium hydroxide, and calcium carbonate (10).



Recently, however, a large deposit of *rasorite* ( $\text{Na}_2\text{B}_4\text{O}_7 \cdot 4\text{H}_2\text{O}$ ) has been discovered in California and has replaced colemanite as the raw material. The rasorite is dissolved in water by heat and pressure, filtered, and a pure borax (11) is crystallized out.



<sup>1</sup> Badger and Baker: Inorganic Chemical Technology, 2nd ed., p. 213, McGraw-Hill Book Co.

<sup>2</sup> Chas. G. Yale, Chem. Zeit. 43, 29 (1905).

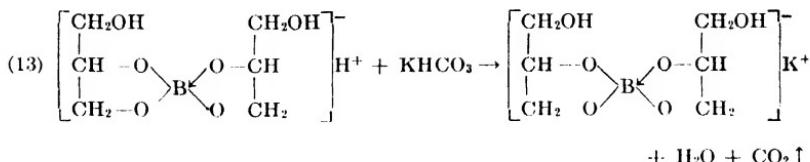
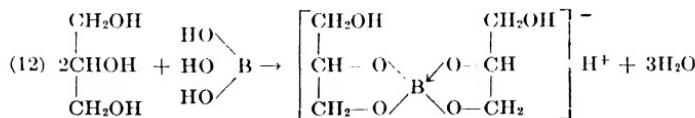
**Pharmaceutical Preparations and Uses.**—1. *Sodium Borate* (Sodi<sup>um</sup> Boras, Borax, Sodium Tetraborate, Sodium Biborate, Sodium Pyroborate), U. S. P. XIII.—Sodium Borate “contains not less than 52.3 per cent and not more than 54.9 per cent of Na<sub>2</sub>B<sub>4</sub>O<sub>7</sub> corresponding to not less than 99 per cent of Na<sub>2</sub>B<sub>4</sub>O<sub>7</sub> · 10H<sub>2</sub>O.” This salt is not used *internally* to any extent because it has been shown to be of no value in the treatment of such diseases as cystitis or (with bromides) epilepsy. Although borax is a fair antiseptic, its use in food products as a preservative has been prohibited by the Food and Drug Administration on the grounds that it is too toxic for internal use.

Sodium borate is used *externally*, however, for (1) eye-washes in 1 to 2 per cent concentrations and (2) as wet dressings for wounds. It is claimed that its action is more bacteriostatic than bactericidal.

Borax is used for “softening” water. It is employed in making hard glass, glazes and enamels. Because it forms fusible salts with oxides of many metals, the calcined salt is used extensively as a flux in welding and soldering.

2. *Rose Water Ointment* (Unguentum Aquæ Rosæ), U. S. P. XIII.—In addition to other ingredients this ointment contains 0.5 per cent of sodium borate. The solution of borax is alkaline and hence saponifies a part of the expressed oil of almonds also present, making a whiter finished preparation. It is used as a “skin food” and cold cream, and on occasion as a base for medicated ointments.

3. *Alkaline Aromatic Solution* (Liquor Aromaticus Alkalinus), N. F. VIII.—Twenty Gm. of sodium borate are used in the preparation of 1000 cc. of the finished preparation, together with 100 cc. of glycerin and 20 Gm. of potassium bicarbonate. Because the sodium borate forms boric acid when dissolved in water (2), and because boric acid reacts with glycerin to form a monobasic acid (see Boric Acid, p. 100) the reactions which take place in manufacturing this preparation can probably be expressed by the following equations (12, 13):



This preparation closely resembles the proprietary preparation “glycothymoline.” It is used as a nasal douche or as a gargle.

For oral use—undiluted; or, for use in a dental spray bottle, dilute with 5 volumes of water.

4. *Compound Sodium Borate Solution* (*Liquor Sodii Boratis Compositus*, Dobell's Solution), N. F. VIII.—This solution requires 15 Gm. each of sodium borate and sodium bicarbonate together with 3 cc. of liquefied phenol and 35 cc. of glycerin to make 1000 cc. of the preparation, the solution being made up to volume with distilled water. The reactions which take place here are probably the same as those taking place above (in Aromatic Alkaline Solution) with the exception that sodium bicarbonate is used in place of potassium bicarbonate. This solution is used as an alkaline antiseptic although the concentrations of active ingredients are hardly sufficient to make them effective. Because of its non-irritating properties it is particularly valuable for use on mucous membranes. The mixed ingredients can be purchased in tablet form. These are convenient in preparing small quantities of the solution. For use on mucous membranes—undiluted; or, for the dental spray bottle, diluted with 5 volumes of water.

### SODIUM BROMIDE .

*Sodium Bromide*, U. S. P. XIII

Formula, NaBr. Molecular Weight, 102.91

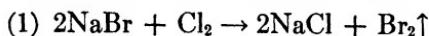
**Physical Properties.**—Sodium Bromide occurs in colorless or white cubical crystals, or as a white, granular powder. It is odorless and has a saline, slightly bitter taste. Sodium bromide slowly takes up moisture from the air without deliquescing. At temperatures below 30° C. the salt crystallizes with 2 molecules of water of hydration in the monoclinic system. At temperatures above 30° C., it forms anhydrous crystals belonging to the regular system. These facts probably account for its property of absorbing moisture from the air without deliquescing. Its specific gravity is about 3.014.

One Gm. of Sodium Bromide dissolves in 1.1 cc. of water and in 16 cc. of alcohol, at 25° C. One Gm. is soluble in 0.8 cc. of boiling water and in 11 cc. of boiling alcohol.

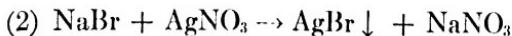
The salt melts at 768° C., and at higher temperatures is slowly volatilized with partial decomposition.

**Chemical Properties.**—Inasmuch as the chemistry of the sodium ion has been discussed (*q. v.*), it only remains to consider the chemistry of the bromide ion to clarify the chemistry of sodium bromide.

The bromide ion, in general, is easily oxidized by molecular chlorine (Cl<sub>2</sub>) to free bromine (Br<sub>2</sub>). This follows the general rule that halogens will displace other halogens of greater atomic weight from their binary salts (1). Other substances such as potassium permanganate, nitric acid and concentrated sulfuric acid will also oxidize bromides and liberate bromine.



The bromide ion may be precipitated as an insoluble bromide by soluble salts of Ag, Hg(ous), Cu(ous) and Pb(ic). For example, sodium bromide solution will yield a precipitate of silver bromide with silver nitrate (2).



Sodium bromide is the salt of a strong acid and a strong base and, therefore, when in solution it is not appreciably hydrolyzed. This accounts for the fact that it is neutral or only slightly alkaline when in solution. The slight alkalinity may be accounted for by the fact that hydrobromic acid is weaker as an acid than sodium hydroxide is as a base. This slight alkalinity is sometimes held to be the cause of precipitation of alkaloids from concentrated solutions of sodium bromide.

**Official Tests for Identity.**—1. The salt responds to all of the tests for *Sodium ion* (*q. v.*).

2. It also responds to all of the tests for *Bromide ion*.

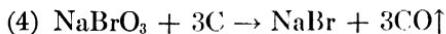
A. The addition of chlorine T.S., dropwise, liberates bromine from aqueous solutions of sodium bromide (1). By shaking the aqueous solution containing the liberated bromine with a small amount of chloroform the bromine may be dissolved from the water and will show up in the chloroform as a red to reddish-brown color.

B. Solutions of sodium bromide will precipitate AgBr (2) with a silver nitrate T.S., the precipitate being insoluble in nitric acid, but slightly soluble in ammonia T.S.

**Commercial Manufacture.**—Most of the sodium bromide made commercially is prepared by adding a slight excess of bromine to a solution of sodium hydroxide to form a mixture of bromide and bromate (3).



The reaction mixture is evaporated to dryness and the solid residue is reduced with carbon to convert the sodium bromate to sodium bromide (4).



As will become increasingly apparent, this general method is used to advantage in the preparation of other bromides from bromine, and of iodides from iodine.

Searle's Lake brine is said to be a potential commercial source of sodium bromide, although the principal production scheme is built around the recovery of potassium chloride and borax.<sup>1</sup>

**Pharmaceutical Preparations and Uses.**—1. *Sodium Bromide* (*Sodii Bromidum*), U. S. P. XIII.—Sodium Bromide, when dried at 110° C. for six hours, contains not less than 99 per cent of NaBr. Sodium bromide is used solely for the effect of the bromide ion, namely as a sedative (see p. 91). It has been recommended by some that

<sup>1</sup> Robertson, G. Ross. Expansion of the Trona Enterprise, *J. Ind. and Eng. Chem.*, 34, 133 (1942)

sodium bromide be substituted for all other bromides inasmuch as it provides the action of the bromide ion in a relatively non-toxic form. Whether this suggestion is worthwhile is debatable. Average dose—1 Gm. (approximately 15 grains).

2. *Five Bromides Elixir* (*Elixir Bromidorum Quinque*), N. F. VIII.—This elixir contains 8.7 per cent of sodium bromide together with varying concentrations of potassium, calcium, lithium and ammonium bromides as the active sedative components. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Bromides Syrup* (*Syrupus Bromidorum*), N. F. VIII.—Bromides Syrup contains 8 per cent of sodium bromide together with the same bromides as found above in Five Bromides Elixir but in slightly different amounts. Average dose—4 cc. (approximately 1 fluidrachm).

4. *Three Bromides Elixir* (*Elixir Bromidorum Trium*), N. F. VIII.—This elixir contains 8 per cent each of sodium, potassium and ammonium bromides. Average dose—4 cc. (approximately 1 fluidrachm).

5. *Three Bromides Tablets* (*Tabellæ Bromidorum Trium*, Triple Bromides Tablets), N. F. VIII.—These tablets “(consisting of ammonium bromide, potassium bromide, and sodium bromide in equal proportions) show a content of bromine not less than 70 per cent and not more than 81 per cent of the labeled amount of total bromides, including all tolerances. The tablets show a content of ammonium bromide not less than 30.8 per cent and not more than 35.8 per cent of the labeled amount of total bromides.” Average dose—0.3 Gm. (approximately 5 grains) each of Ammonium Bromide, Potassium Bromide, and Sodium Bromide.

6. *Sodium Bromide Elixir* (*Elixir Sodii Bromidi*), N. F. VIII.—This elixir “contains, in each 100 cc., not less than 16.5 Gm. and not more than 18.5 Gm. of NaBr.” Average dose—4 cc. (approximately 1 fluidrachm).

7. *Sodium Bromide Tablets* (*Tabellæ Sodii Bromidi*), N. F. VIII.—These tablets “contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of NaBr.” Average dose—1 Gm. (approximately 15 grains) of Sodium Bromide.

### SODIUM CACODYLATE. (See p. 527.)

### SODIUM CARBONATE

#### *Monohydrated Sodium Carbonate*, U. S. P. XIII

Formula,  $\text{Na}_2\text{CO}_3 \cdot \text{H}_2\text{O}$ . Molecular Weight, 124.02

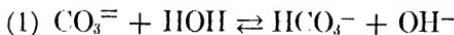
**Physical Properties.**—Monohydrated Sodium Carbonate is a white, orthorhombic, crystalline or granular powder. It is odorless and has a strong alkaline taste. The salt absorbs a small amount of moisture from the air, but in warm, dry air at 50° C. or above it effloresces, becoming anhydrous at 100° C. Anhydrous sodium

carbonate melts at 853° C., at which temperature it loses a small quantity of carbon dioxide. It is decomposed at very high temperatures.

One Gm. of Monohydrated Sodium Carbonate dissolves in 3 cc. of water and in 7 cc. of glycerin, at 25° C. One Gm. is soluble in 1.8 cc. of boiling water. It is insoluble in alcohol.

**Chemical Properties.**—The chemistry of sodium carbonate may be considered advantageously in three major divisions, namely, (a) hydrolysis reactions, (b) hydration and (c) other reactions.

(a) Sodium carbonate, when dissolved in water imparts a highly alkaline reaction to the water as evidenced by the fact that the pH of a molar solution is 11.6. This is due to the hydrolysis which takes place in aqueous solutions of it. The hydrolysis is due to the fact that the carbonate ion is a fairly strong base (see Lowry-Brörsted Concept of Acids and Bases, p. 34) (1).



A further hydrolysis takes place (2) to a lesser extent wherein another mole of OH<sup>-</sup> is formed.



The accumulation of OH<sup>-</sup> accounts for the alkalinity exhibited by the solution.

(b) Sodium carbonate is interesting from the standpoint that it forms at least 3 well-characterized hydrates besides the anhydrous salt. These are:

1. Monohydrate = Na<sub>2</sub>CO<sub>3</sub>.H<sub>2</sub>O
2. Heptahydrate = Na<sub>2</sub>CO<sub>3</sub>.7H<sub>2</sub>O
3. Dekahydrate = Na<sub>2</sub>CO<sub>3</sub>.10H<sub>2</sub>O

Figure 12 shows graphically the forms which are in equilibrium with the saturated solution at different temperatures.

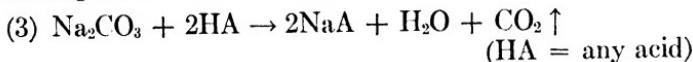
At temperatures above 35° C. a saturated solution will deposit only the monohydrated form. If the hot saturated solution is allowed to cool in an atmosphere free of dust it is often possible to obtain the heptahydrate crystals. However, if the solution cools below 33° C. the dekahydrate forms because the heptahydrate is more soluble than the dekahydrate. It is interesting to note that the maximum solubility of sodium carbonate is at approximately 35° C.

Commercial anhydrous sodium carbonate is known as *soda ash*, whereas the dekahydrate is commonly known as *sal soda*, *washing soda*, or *soda crystals*. The dekahydrate is prone to *effloresce* under conditions of storage. *Efflorescence* is the term used to denote the loss of water of crystallization from a compound at room temperature. It is explained on the basis that every salt containing water of crystallization has a certain vapor pressure. If the vapor pressure exerted by the water of crystallization is greater than that exerted by the moisture in the air then the compound will

lose water to the air until equilibrium has been established or until all available water is gone.

(c) Sodium carbonate enters into many reactions such as *neutralization*, *double decomposition*, *precipitation* and *saponification*.

Sodium carbonate, in solution or in the solid form, is capable of neutralizing acids with the formation of a salt,  $\text{CO}_2$  and  $\text{H}_2\text{O}$  (3).



Cold solutions of sodium carbonate, when treated with carbon dioxide will form the bicarbonate (3a), which may be regarded as essentially a half neutralization of sodium carbonate with carbonic acid (formed by interaction of  $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3$ ).

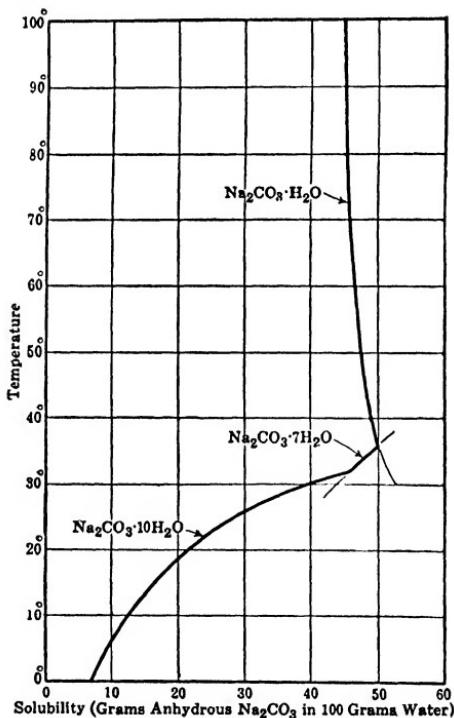
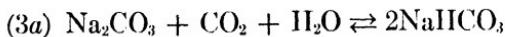
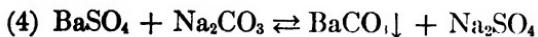


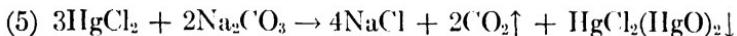
FIG. 12.—Solubility Curve for Sodium Carbonate, (Reprinted by permission from Synthetic Inorganic Chemistry, by Blanchard, Phelan and Davis, published by John Wiley & Sons, Inc.)

Sodium carbonate is used in qualitative analysis because of its ability to decompose difficultly soluble precipitates such as  $\text{BaSO}_4$ ,  $\text{PbSO}_4$ ,  $\text{CaSO}_4$  and  $\text{SrSO}_4$ . For example, barium sulfate is decomposed (although with difficulty) by boiling or fusing it with sodium carbonate (4).



Although  $\text{BaSO}_4$  is difficult to decompose, the other sulfates mentioned are almost completely decomposed by this treatment.

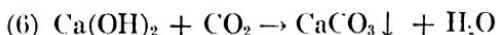
Since the only normal carbonates which are freely soluble are those of the alkali metals and ammonium, it is possible to use sodium carbonate, for example, as a reagent to precipitate the insoluble carbonates of the other metals. Thus, we find that silver nitrate, and also barium chloride, form insoluble carbonates with an aqueous solution of sodium carbonate. Although this might seem to be the case with mercuric chloride, this does not occur, inasmuch as mercuric chloride T.S. when added to an aqueous solution of the salt immediately precipitates a reddish-brown precipitate of a basic salt (5).



Because sodium carbonate is alkaline in solution it is used to some extent as a saponifying agent for fats and oils both in pharmaceutical practice and elsewhere. For example, a fat such as *stearin*, which is a glyceryl ester of a fatty acid, will be hydrolyzed or saponified by sodium carbonate (see also Sodium Hydroxide, p. 189) to yield glycerin and a soap (a metallic salt of a fatty acid; in this case the sodium salt). This saponifying action of sodium carbonate has led to the use of its preparations as detergents for removing grease in many industrial operations. Often, however, the alkalinity imparted by the sodium carbonate is too high. In these cases, it is possible to purchase various admixtures of the sodium carbonate with sodium bicarbonate which are less alkaline. One common preparation of this type is *sodium sesquicarbonate*,  $\text{Na}_2\text{CO}_3 \cdot \text{NaHCO}_3 \cdot 2\text{H}_2\text{O}$ .

**Official Tests for Identity.**—1. A solution of Monohydrated Sodium Carbonate (1 in 10) is strongly alkaline to litmus paper and to phenolphthalein T.S. for the reasons cited under "Chemical Properties." This distinguishes it from sodium bicarbonate which either does not color phenolphthalein or does so only slightly.

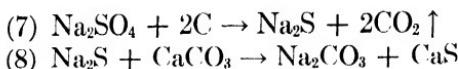
2. The salt responds to all of the tests for *Sodium* (*q. v.*).
3. The salt responds to all of the tests for *Carbonate ion*: Sodium carbonate effervesces with acids (3) to liberate  $\text{CO}_2$  which will cause a precipitate of calcium carbonate if passed through lime water (6).



**Commercial Manufacture.**—Sodium carbonate is or has been obtained by (1) the LeBlanc Process, (2) the Cryolite-Soda Process, (3) the Solvay Process, and (4) recovery from natural brine.

1. LeBlanc, in 1790, devised a method for converting salt into sodium carbonate. Up to this time the world supply of alkali was from natural sources or from wood ashes. Although this method was never introduced into the United States it attained great popularity in Europe and during the nineteenth century was responsible for practically the world's supply of alkali. The follow-

ing general reactions are thought to occur in the furnace (commonly known as a "black-ash" furnace) (7, 8).

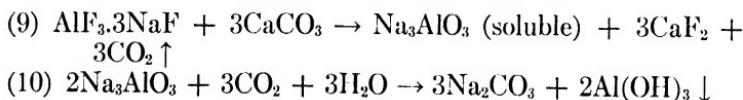


Salt cake, obtained in the manufacture of hydrochloric acid (see p. 110), limestone crushed to about the size of "pea coal," and finely crushed coal constitute the raw materials. After being heated in the furnace, the product, known as "black ash," is cooled and lixiviated in a series of tanks arranged so as to permit of continuous extraction. When concentrated, the solution deposits salt soda crystals (sometimes known as "black salt"). These are then calcined to rid them of water, organic matter, etc., and then ground in mills.

This process is obsolete because it has been superseded by the Solvay process which is more economical and produces a much purer product.

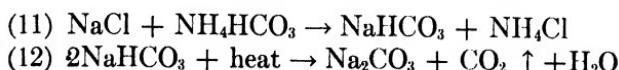
*2. Cryolite-soda Process.*—Soda may be obtained from a mineral known as *cryolite*, a double fluoride of sodium and aluminum ( $\text{AlF}_3 \cdot 3\text{NaF}$ ), which occurs in large quantities in Denmark and in the southern part of Greenland. In the early part of the nineteenth century, Julius Thomsen, a Dane, first considered this mineral as a possible source of sodium carbonate. In 1854 he obtained the exclusive right to mine the cryolite and work it up into soda. He later sold his rights to an American company.

To obtain sodium carbonate the finely powdered mineral is mixed with limestone and calcined at red heat in a reverberatory furnace (9). The mass is never allowed to fuse on account of the difficulty encountered in the subsequent lixiviation of such a mass. After lixiviation, the solution is carbonated with carefully washed lime-kiln gases (10). During the carbonation the solution is kept hot, thereby assuring a granular precipitate of aluminum hydroxide, from which it is comparatively easy to wash out the soda. Solutions at ordinary temperature yield a gelatinous precipitate of aluminum hydroxide which is practically impossible to handle. The solution of sodium carbonate is evaporated and the salt allowed to crystallize.



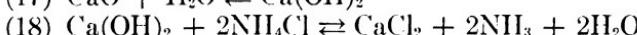
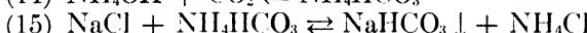
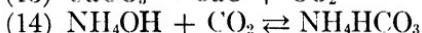
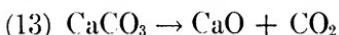
This process is likewise obsolete having been replaced by the Solvay Process.

*3. Solvay Ammonia-soda Process.*—In 1838, H. G. Dyar and J. Hemming took out an English patent for making sodium carbonate by means of a reaction well known at that time (11 and 12).



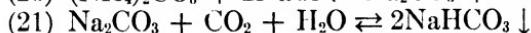
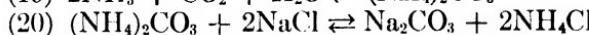
In 1863, Ernest Solvay, a Belgian, began to develop a commercial method for making sodium carbonate from sodium chloride, ammonia, and carbon dioxide. Although unfamiliar with most of the previous work that had been done upon it, he overcame the mechanical difficulties and made it a commercial success in 1873. Since that time it has been growing in importance until at present most of the world's supply of soda is made by the Solvay process.

In brief, the process consists in passing carbon dioxide, which has been prepared either by burning limestone using coke or by calcining sodium bicarbonate (13) (16), into ammonium hydroxide to form ammonium bicarbonate (14). When the latter is mixed with a solution of sodium chloride, sodium bicarbonate is precipitated and ammonium chloride remains in solution (15). The sodium bicarbonate is collected and then calcined and the evolved carbon dioxide is cooled and used over again (16). The ammonium chloride is treated with milk of lime (17) and the evolved ammonia is led back into the system (18). The solution of calcium chloride so formed is usually run to waste or evaporated for commercial uses.



In the actual process, the number of required steps is less than the foregoing equations would indicate, because the sodium chloride solution (brine) is first saturated with ammonia and then carbon dioxide passed through the mixture (14) and (15). At a lowered temperature sodium bicarbonate separates out. It will be noted that the reaction (15) between the sodium chloride and ammonium bicarbonate is a reversible one. Therefore, the reaction can never go to completion, although it can be driven in the desired direction by having an excess of sodium chloride present.

Although the reactions involved in the Solvay Process are usually represented as above, there is some disagreement<sup>1</sup> as to the exact mechanism whereby the end-product is reached. In brief, it is pointed out that the supposition of ammonium bicarbonate as an intermediate is irrational because (1) ammonium bicarbonate is just as sparingly soluble as sodium bicarbonate in the mother liquors and would itself be precipitated, and (2) such a reaction would be endothermal, whereas the actual reaction is exothermal. The suggested mechanism is as follows (19, 20, 21):



<sup>1</sup> See Mellor's Modern Inorganic Chemistry, revised edition by Parkes and Mellor, Longmans, Green & Co., p. 558, 1939.

**Pharmaceutical Preparations and Uses.**—1. *Monohydrated Sodium Carbonate* (Sodii Carbonas Monohydratus), U. S. P. XIII.—Monohydrated Sodium Carbonate, when dried at 110° C. to constant weight, contains not less than 99.5 per cent of  $\text{Na}_2\text{CO}_3$ . This is the only sodium carbonate which is official, although the anhydrous form is required as a buffer in Sterile Thiopental Sodium. Sodium carbonate may be given internally for the same conditions for which sodium bicarbonate is employed. However, it is seldom used because of its marked alkalinity and irritating properties. Solutions of sodium carbonate are employed as lotions in certain skin diseases, such as scaly eruptions, psoriasis, etc. They tend to dissolve skin oils and also the horny matter on the skin surface thus softening the skin.

This salt is used more for its alkalinity in making various pharmaceutical preparations than it is in therapy.

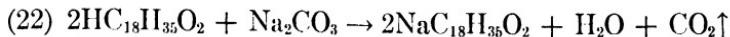
2. *Sterile Thiopental Sodium* (Thiopentalum Sodicum Sterile, Sterile Thiopentone Soluble), U. S. P. XIII.—“Sterile Thiopental Sodium is a mixture of thiopental sodium with anhydrous sodium carbonate as a buffer. It contains not less than 84 per cent and not more than 87 per cent of thiopental ( $\text{C}_{11}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$ ), calculated on a moisture-free basis, corresponding to not less than 91.7 per cent of  $\text{C}_{11}\text{H}_{17}\text{N}_2\text{O}_2\text{SNa}$ .” Since anhydrous sodium carbonate is not official except as a reagent, this preparation is considered here. It is used for its hypnotic effect and is usually administered intravenously. During World War II this drug was a favorite anesthetic in the warm countries where the gaseous anesthetics were difficult to administer. It was frequently referred to as the “needle anesthetic.” Average dose—for anesthesia—to be determined by the physician according to the needs of the patient.

3. *Ferrous Carbonate Mass* (Massa Ferri Carbonatis, Vallet’s Mass), N. F. VIII.—“Ferrous Carbonate Mass contains not less than 36 per cent and not more than 41 per cent of  $\text{FeCO}_3$ .” The N. F. requires 460 Gm. of Monohydrated Sodium Carbonate to be reacted with 1000 Gm. of Ferrous Sulfate to prepare 1000 Gm. of the finished product. The function of the sodium carbonate is, of course, to furnish the carbonate ion for the synthesis of ferrous carbonate. (For a further discussion see Ferrous Carbonate, p. 682.) Average dose—0.6 Gm. (approximately 10 grains).

4. *Nitromersol Solution* (Liquor Nitromersolis), N. F. VIII.—The preparation of 1000 cc. of this solution requires the use of 4.25 Gm. of Monohydrated Sodium Carbonate together with 0.4 Gm. of sodium hydroxide. These two alkalies are used to dissolve the water-insoluble Nitromersol by opening its anhydride ring and forming the sodium salt which is water-soluble. The N. F. cautions: “*Dilutions of Nitromersol Solution should be prepared as needed as they tend to precipitate upon standing.*” This preparation is an efficient antiseptic.

5. *Solid Soap Liniment* (Linimentum Saponis Spissum, Camphorated Soap Liniment, Solid Opodeldoc), N. F. VIII.—Ten Gm. of

Monohydrated Sodium Carbonate are required together with other ingredients to prepare 1000 cc. of the finished product. The sodium carbonate reacts with the stearic acid present to form the sodium stearate (22) soap.



(Stearic acid is a mixture of stearic and palmitic acids, but the above will suffice to explain the reaction.) This preparation is used externally as a liniment, since it has rubefacient and irritant properties.

### SODIUM CHLORIDE

#### *Sodium Chloride, U. S. P. XIII*

Formula, NaCl. Molecular Weight, 58.45

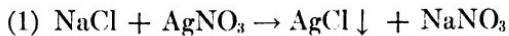
**Physical Properties.**—Sodium Chloride occurs in the form of colorless, transparent, cubical crystals, or as a white crystalline powder. When crystallized from dilute solutions it forms hollow quadratic pyramids. When saturated solutions of sodium chloride are cooled to  $-10^{\circ}$  C., large monoclinic tablets of  $\text{NaCl} \cdot 2\text{H}_2\text{O}$  separate out. At  $0^{\circ}$  C. these tablets lose water and are converted into cubes. The salt is odorless, has a saline taste, and a specific gravity of 2.163. Usually it is slightly hygroscopic, due to the presence of small amounts of magnesium or calcium chloride.

Sodium chloride is only slightly more soluble in boiling water than it is in cold water, 1 Gm. dissolving in 2.8 cc. of water at  $25^{\circ}$  C. and in 2.7 cc. of boiling water. One Gm. is soluble in 10 cc. of glycerin, at  $25^{\circ}$  C. It is slightly soluble in alcohol and insoluble in hydrochloric acid.

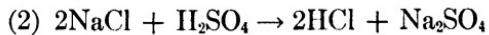
When heated somewhat above  $100^{\circ}$  C., the salt decrepitates because of the evaporation of the interstitial water enclosed by the small crystals. It fuses at about  $804^{\circ}$  C., boils at  $1413^{\circ}$  C., and at white heat slowly volatilizes with partial decomposition.

**Chemical Properties.**—Most of the chemical properties of sodium chloride, which are of importance pharmaceutically, may be attributed to the chloride ion.

Chlorides of almost all of the metals are water-soluble with the notable exception of  $\text{AgCl}$ ,  $\text{HgCl}$  and  $\text{PbCl}_2$ . Therefore, solutions of sodium chloride will produce precipitates with soluble silver, mercurous, and lead salts (1).

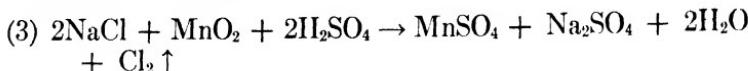


Sodium chloride reacts readily with fixed acids such as sulfuric (2) and phosphoric acids to liberate hydrogen chloride. This, of course, is the basis for the preparation of hydrochloric acid from salt (see p. 110).



Sodium chloride is rather easily oxidized to liberate free chlorine, the oxidation being carried out either *chemically* or *electrolytically*.

The chemical oxidation of sodium chloride may be illustrated by the addition of concentrated sulfuric acid and  $\text{MnO}_2$  to the chloride (3) to liberate free chlorine.



The electrolytic oxidation of sodium chloride may be carried out on the anhydrous fused salt (see Manufacture of Sodium, p. 147), or it may be carried out on an aqueous solution of sodium chloride (see Manufacture of Chlorine, p. 85).

**Official Tests for Identity.**—1. A solution of sodium chloride gives all of the tests for *Sodium* ion (*q. v.*).

2. Sodium chloride solutions also respond to all of the tests for *Chloride* ion.

(a) They yield a precipitate of  $\text{AgCl}$  with silver nitrate T.S. (1). This precipitate is insoluble in an excess of nitric acid, but is soluble in an excess of ammonium hydroxide (see p. 110).

(b) When warmed with potassium permanganate and diluted sulfuric acid, solutions of sodium chloride will evolve the characteristic odor of chlorine (4).



**Commercial Manufacture.**<sup>1</sup>—Sodium chloride is found in all parts of the world either in the form of natural deposits, such as those of Stassfurt, Reichenhall, Cheshire, New York, Kansas, Colorado, Louisiana, Utah, California, Michigan and many other districts; or in solution in sea, lake, spring, or natural or made wells. It is an absolute necessity to man and beast; aiding in the absorption of albuminoid materials and, by dissociation, no doubt supplying the chloride ion for the hydrochloric acid of the gastric juice.

In Germany, Louisiana, and elsewhere, it is mined as rock salt. Shafts are sunk to the bed and long galleries, often a mile in length, are run out. The salt is undercut and blasted down with low-power dynamite. It is then crushed in roller mills and screened to obtain the various sizes. In one Colorado deposit the salt occurs in the form of a crust over an underground lake of brine. This is worked by removing the earth, cutting the crusted salt like ice, washing it in the brine, and then crushing, as previously described, in mills.

In other deposits, *e. g.*, those of New York, Ohio, Michigan, etc., the salt is found either mixed with clay or organic matter, or the locations of the beds are such as to make mining very impractical. In such places, wells are sunk, the salt dissolved in water, and the resulting brine pumped to the surface.

<sup>1</sup> Badger and Baker: *Inorganic Chemical Technology*, 2nd ed., McGraw-Hill Book Co., p. 6, 1941.

In California and in the hot countries around the Mediterranean basin, salt is obtained from sea-water (containing about 3 per cent sodium chloride) by concentrating it in very large, shallow ponds connected in series. The heat from the sun is sufficient to effect the evaporation of the water. At high tide the sea-water is allowed to flow into the first basin where the less soluble material and suspended matter (calcium carbonate, clay, gypsum, organic substances etc.) precipitate out. It then goes to the so-called crystallizing ponds, where it is evaporated to about 25° Baumé. Here the crystallized salt separates out. In the succeeding pans, the more soluble salts, *e. g.*, magnesium sulfate, magnesium chloride, sodium sulfate, potassium chloride, and varying quantities of potassium iodide and bromide (bittern) are obtained.

In northern Russia, Norway, and other cold countries the sea-water is concentrated by freezing the water in basins and pumping out the residual liquid part which contains all of the salt.

All sodium chloride that has been obtained from its natural source in the form of brine must be purified. The methods in use are many, and depend largely upon the character of the impurities present in a particular brine. Calcium and magnesium salts are the usual impurities and may be removed by treating the brine with either soda ash and lime or soda ash and caustic soda, and allowing the precipitate to settle.

The purified brine is concentrated in long, narrow, shallow pans fitted with steam pipes extending the entire lengths of the pans and supported some distance above the bottom of the pans. These pans are called "grainers" and are from 50 to 100 feet long and from 10 to 25 feet wide. As the salt crystals form on the pan bottom, they are raked out automatically onto a sloping drain board on one end of the pan. Triple-effect vacuum pans are also used for concentrating and crystallizing the salt. Free acid, formed by the hydrolysis of the magnesium salts, seriously corrodes the pipes in the vacuum concentrators and scale forms on the steam pipes if the salt has not been sufficiently purified.

The purest form of salt is now obtained by passing hydrogen chloride into a saturated solution of salt, and mechanically "fishing out" the crystals as they form. The crystals so obtained are centrifuged and dried. When highly soluble hydrogen chloride is passed into a saturated solution of sodium chloride it forms a concentrated solution of hydrochloric acid in which the sodium chloride is only slightly soluble. The slight solubility of sodium chloride in solutions saturated with hydrogen chloride is accounted for by the fact that hydrogen chloride, when dissolved in water, forms hydrates which, of course, reduce the amount of water available for dissolving sodium chloride. It is comparable to having removed an equivalent number of water molecules from the solution by evaporation, etc.

**Laboratory Preparation of Pure Sodium Chloride.**<sup>1</sup>—Dissolve 25 Gm. of rock salt in 75 cc. of water, hastening the action with gentle heating. To the solution add about 1 Gm. of sodium carbonate dissolved in a few cc. of water. Stir, let settle, and add a few drops more of sodium carbonate solution, and if no fresh precipitate is produced in the clear part of the solution no more need be added; otherwise enough more must be added to produce this result. Filter the hot solution, through an ordinary filter. Prepare pure hydrogen chloride by placing 50 Gm. of rock salt in the generator flask and

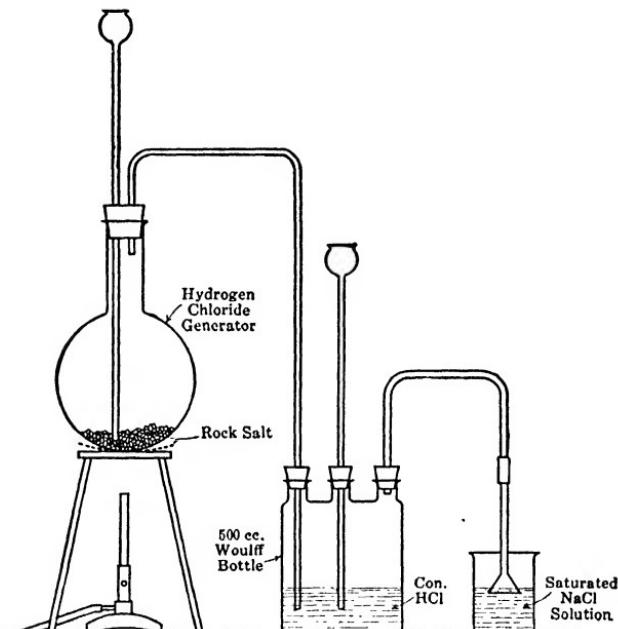


FIG. 13.—Apparatus for Preparing Pure Sodium Chloride. (Reprinted by permission from Synthetic Inorganic Chemistry, by Blanchard, Phelan and Davis, published by John Wiley & Sons, Inc.)

treating it with 95 cc. of concentrated sulfuric acid. The gas is purified by bubbling it through a washing bottle containing about 110 cc. of concentrated hydrochloric acid, and then it is passed through the wide-mouthed funnel into the sodium chloride solution in a 600-cc. beaker. When hydrogen chloride ceases to be evolved by the generator, collect the precipitated sodium chloride on a suction filter. Test the filtrate for sulfate by adding a little barium chloride T.S. to a small sample of it diluted with water. A positive test will probably be obtained. Now wash the crystals with successive portions of 10 cc. of 18 per cent hydrochloric acid, until the washings show no further test for sulfates. Then transfer the crystals to a porcelain dish and heat gently, while stirring, until all decrepitation ceases. Bottle the product.

<sup>1</sup> Blanchard, Phelan and Davis: Synthetic Inorganic Chemistry, John Wiley & Sons, p. 189, 1936.

**Pharmaceutical Preparations and Uses.**—1. *Sodium Chloride* (Sodii Chloridum), U. S. P. XIII.—Sodium Chloride, when dried at 110° C. for two hours, contains not less than 99.5 per cent of NaCl. Sodium chloride exerts the effect of the chloride ion (see p. 86), as well as the effect of the sodium ion (see p. 147). It occurs in all of the fluids and nearly all of the tissues of the body. When introduced into the stomach in moderate amounts, it produces very little effect. However, a deficiency of sodium and chloride ions in the body results in the phenomena of "salt hunger," expressed in metabolic disturbances, emaciation, etc.

Sodium chloride, in 20 per cent solution, is used to some extent for the injection treatment of varicose veins of the lower extremities. The solution, in amounts up to 5 or 10 cc. is injected into the lumen of the vein to bring the concentrated solution into intimate contact with the wall of the vein.

In the last decade or so, numerous articles have appeared in pharmaceutical and medical journals about the importance of making eye solutions with the same osmotic pressure as that of the lachrymal fluid. The lack of interest shown in this subject by both physicians and pharmacists may be attributed to the fact that the calculations involved for preparing isotonic solutions have been rather technical and time-consuming. However, in recent years the method of calculation has been simplified to the point where it is only a matter of using simple mathematics with a prepared table of sodium chloride equivalents for the various chemicals. During the last few years this simplified method of calculation has been given wide publicity in pharmaceutical journals and in published articles. (See Appendix for Tables).

It is being increasingly recognized by physicians that solutions coming into close contact with the delicate eye tissue must be isotonic if irritation, pain, and discomfort are to be avoided. There is some disagreement on this point as shown by recent work.<sup>1</sup>

When a pharmacist receives a prescription which reads *Fiat Isotonic Collyrium*, he should be prepared to compound that prescription according to the prescriber's orders.

The varied commercial uses of sodium chloride as well as the large amounts used yearly are illustrated by the fact that 7,157,646 tons were used in 1943 to produce soda ash, 2,656,293 tons for the manufacture of chlorine, 508,050 tons to make other chemicals, and 66,000 tons in the synthetic rubber program.

2. *Dextrose and Sodium Chloride Injection* (Injectio Dextrosi et Sodii Chloridi), U. S. P. XIII.—"Dextrose and Sodium Chloride Injection is a sterile solution of dextrose and sodium chloride in water for injection. It contains not less than 95 per cent and not more than 105 per cent of the labeled amount of  $C_6H_{12}O_6 \cdot H_2O$  and of NaCl." The U. S. P. gives a caution: *The sodium chloride content of this Injection is generally of high concentration. Dextrose and*

<sup>1</sup> Hind and Goyan, J. A. Ph. A., 36, 33 (1947).

*Sodium Chloride Injection containing a sodium chloride concentration corresponding to the sodium chloride content of isotonic sodium chloride solution is to be labeled "Dextrose Injection in Isotonic Sodium Chloride Solution."* This solution is often used for the intravenous introduction of chloride ion.

3. *Phenolsulfonphthalein Injection* (*Injectio Phenolsulfonphthaleini*), U. S. P. XIII.—This injection “is a sterile solution of phenolsulfonphthalein rendered soluble with sodium bicarbonate or sodium hydroxide in isotonic sodium chloride solution made with water for injection. It contains not less than 95 per cent and not more than 105 per cent of the labeled amount of  $C_{19}H_{14}O_5S$ .” The function of the sodium chloride in this preparation is, of course, to furnish an injection vehicle which is isotonic with the blood. Nine Gm. of sodium chloride are required for 1000 cc. of finished preparation. (See also p. 156.)

4. *Ringer's Solution* (*Liquor Ringeri*, Isotonic Solution of Three Chlorides, U. S. P. XII), U. S. P. XIII.—This solution “contains, in each 100 cc., not less than 820 mg. and not more than 900 mg. of NaCl, not less than 25 mg. and not more than 35 mg. of KCl, and not less than 30 mg. and not more than 36 mg. of CaCl<sub>2</sub>.2H<sub>2</sub>O.” The U. S. P. notes that “Unless otherwise specified, No. 3—Sterile Ringer's Solution for Parenteral Use must be dispensed.” The U. S. P. specifies three kinds of Ringer's Solution:

No. 1—Non-sterile Ringer's Solution (prepared from 8.6 Gm. NaCl, 0.3 Gm. KCl and 0.33 Gm. CaCl<sub>2</sub>.2H<sub>2</sub>O per 1000 cc. of solution).

No. 2—Sterile Ringer's Solution Not for Parenteral Use.

No. 3—Sterile Ringer's Solution for Parenteral Use.

The deleterious effects of single-salt solutions, *i. e.*, *Isotonic Sodium Chloride Solution*, U. S. P. XIII, upon excised tissues, were responsible for the production of so-called “balanced solutions,” such as Ringer's Solution. Sterile Isotonic Sodium Chloride Solution, when injected into animals, is rapidly adjusted, insofar as the several ion concentrations are concerned, by exchange with the various tissues. This, however, does not take place with excised tissues and, therefore, the ion concentrations of blood plasma must be simulated as near as possible in order for the solutions to maintain the functions of the excised tissues. Ringer's Solution is one of these balanced solutions in which the calcium ion antagonizes the inhibitory effects of the potassium ion as well as the stimulant effects of the sodium ion. Bacteriostatic agents are not permitted in Ringer's Solution and the pH must fall within the limits of 5 to 7.5.

5. *Lactated Ringer's Solution* (*Liquor Ringeri Lacticus*), U. S. P. XIII.—This solution “is a sterile solution in water for injection containing, in each 100 cc., not less than 18 mg. and not more than 22 mg. of CaCl<sub>2</sub>.2H<sub>2</sub>O, not less than 27 mg. and not more than 33 mg. of KCl, not less than 570 mg. and not more than 630 mg. of NaCl, and not less than 290 mg. and not more than 330 mg. of

$\text{NaC}_3\text{H}_6\text{O}_3$ ." This solution was developed by Alexis F. Hartmann as a "combined solution"—a combination of sodium lactate and hypotonic Ringer's solution. The solution is designed to supply water, base chloride, base bicarbonate, and antiketogenic effect in treating dehydration accompanied by moderate acidosis or alkalosis. Inasmuch as this solution, when given in sufficient amounts brings about relief of moderate acidosis or alkalosis, it obviates the expensive and time-consuming necessity of chemical analysis of the blood to determine whether an acidosis or an alkalosis exists. (See p. 201.)

6. *Isotonic Sodium Chloride Solution* (*Liquor Sodii Chloridi Isotonicius*, *Physiological Sodium Chloride Solution*, *Physiological Salt Solution*, *Normal Saline Solution*), U. S. P. XIII.—"Isotonic Sodium Chloride Solution contains, in each 100 cc., not less than 850 mg. and not more than 950 mg. of  $\text{NaCl}$ ." Just as in Ringer's Solution, there are three Isotonic Sodium Chloride Solutions, namely, (1) *No. 1—Non-sterile Isotonic Sodium Chloride Solution*, (2) *No. 2—Sterile Isotonic Sodium Chloride Solution Not for Parenteral Use*, and (3) *No. 3—Sterile Isotonic Sodium Chloride Solution for Parenteral Use*. The No. 3 solution is to be dispensed in the event that no specification is made.

The title *Hypotonic Sodium Chloride Solution* applies to solutions which contain less than 0.85 Gm. of sodium chloride in each 100 cc. and the title *Hypertonic Sodium Chloride Solution* applies to solutions which contain more than 0.95 Gm. of sodium chloride in each 100 cc., and such solutions should be so labeled when dispensed, and the proportion or the weight of sodium chloride in a given volume must be indicated on the label.

The addition of bacteriostatic agents is not permitted. The Isotonic Sodium Chloride Solution has a pH range from 5 to 7. Isotonic sodium chloride solution may be used intravenously or by hypodermoclysis to amplify the volume of the blood without causing serious osmotic changes, inasmuch as it affects the extracellular fluid only as a diluent. Because of the rapidity with which sodium chloride, water, etc., escape from the circulation during shock conditions, such colloidal substances as acacia are often added to the solutions to prevent this rapid loss, and thus maintain blood volume. It is also often used as an isotonic vehicle for various medicaments to be applied to mucous membranes.

7. *Anticoagulant Sodium Citrate Solution* (*Liquor Sodii Citratis Anticoagulans*), U. S. P. XIII.—This is "a solution of sodium citrate in isotonic sodium chloride solution and contains, in each 100 cc., not less than 2.3 Gm. and not more than 2.7 Gm. of  $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ , and not less than 850 mg. and not more than 950 mg. of  $\text{NaCl}$ ." (See p. 184.)

8. *Thyroid* (*Thyroideum*), U. S. P. XIII.—Since the iodine content of the thyroid gland often varies above the U. S. P. requirement, certain diluents such as a desiccated thyroid of a lower iodine content, lactose, sodium chloride, starch, or sucrose are permitted. Average dose—60 mg. (approximately 1 grain).

9. *Ephedrine Sulfate Solution* (*Liquor Ephedrinæ Sulfatis*), N. F. VIII.—This solution contains 30 Gm. of ephedrine sulfate, 5 Gm. of chlorobutanol, and 3.6 Gm. of sodium chloride in 1000 cc. of finished solution. The function of the sodium chloride in this preparation is to bring up the osmotic equivalent of the solution to approximately an isotonic strength. The amount of sodium chloride used is slightly more than enough to make the solution isotonic, but when it is diluted with isotonic sodium chloride solution as recommended, the difference in the isotonicity of the solution from that of the nasal secretions is practically negligible. For use on mucous membranes—dilute with an equal volume of isotonic sodium chloride solution.

10. *Pectin Paste* (*Pasta Pectini*), N. F. VIII.—Sodium chloride occurs in this preparation as a constituent of Isotonic Three Chlorides Solution (Ringer's Solution). Pectin Paste is sometimes used by itself or with added medicaments for the treatment of burned or abraded surfaces. The use of an isotonic base results in less irritation at the site of application.

11. *Thin Pectin Paste* (*Pasta Pectini Tenuis*), N. F. VIII.—This preparation is the same as the preceding with the exception that the paste is of a thinner consistency.

12. *Procaine Hydrochloride Solution* (*Liquor Procainæ Hydrochloridi*), N. F. VIII.—Sodium chloride occurs in this preparation as a constituent of Isotonic Sodium Chloride Solution. Twenty Gm. of procaine hydrochloride is dissolved in sufficient isotonic solution to make 1000 cc. of the finished preparation. The function of the sodium chloride, of course, is to provide isotonicity for a solution which is to be used by injection. Non-isotonic solutions induce pain. Average parenteral dose—1 cc.

13. *Sodium Chloride Tablets* (*Tabellæ Sodii Chloridi*), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 105 per cent of the labeled amount of NaCl." These tablets are available usually in 5-,  $7\frac{1}{2}$ -, 10- and 15-grain sizes. They are often used to replace the sodium chloride lost through excessive perspiration in hot weather. It is said<sup>1</sup> that the use of tablets of sodium chloride is inferior to the use of salted water (0.1 to 0.2 per cent) in that the tablets are more apt to cause nausea and vomiting through gastric irritation. One Gm. of sodium chloride dissolved in a quart of water makes 0.1 per cent solution which may be used for this purpose. (See also Sodium Chloride and Dextrose Tablets immediately following.)

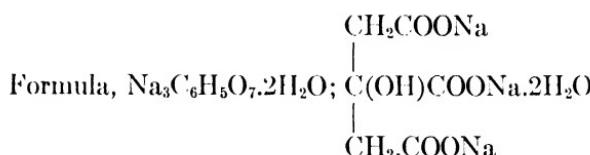
14. *Sodium Chloride and Dextrose Tablets* (*Tabellæ Sodii Chloridi et Dextrosi*), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amounts of NaCl and of  $C_6H_{12}O_6 \cdot H_2O$ ." These tablets have been designed as a means of administering sodium chloride during hot weather. The sodium chloride, as stated above, replaces the salt

<sup>1</sup> A. M. A. Council on Pharmacy and Chemistry Reports, p. 7 (1945).

lost through perspiration, whereas the dextrose is said to supply a quickly available source of energy. The commercial tablets on the market usually contain 7 grains of salt and 3 grains of dextrose per tablet. The recommended dose (of the commercial preparation) is 5 to 10 tablets daily, to be taken one at a time with a glass of water. Although the administration of sodium chloride is rational enough it seems as if the inclusion of dextrose in the tablets for the purpose of supplying energy has little, if any, merit, inasmuch as 10 such tablets would contain only 30 grains (2 Gm.) of dextrose. This amount would seem to fall far short of the energy requirements during hot weather.

## SODIUM CITRATE

*Sodium Citrate*, U. S. P. XIII

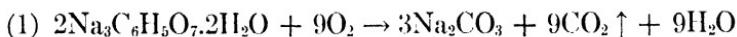


### Molecular Weight, 294.12

**Physical Properties.**—Sodium Citrate occurs in colorless, monoclinic crystals or as a white, odorless, crystalline powder, having a cool, saline taste. The salt slowly effloresces on exposure to dry air.

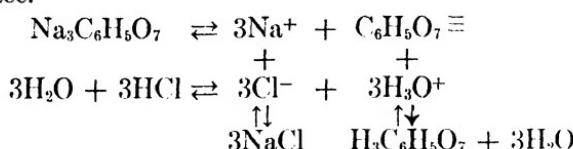
One Gm. of the salt dissolves in 1.5 cc. of water at  $25^{\circ}\text{ C}$ . and in 0.6 cc. of boiling water. It is insoluble in alcohol.

**Chemical Properties.**—When heated to  $100^{\circ}$  C., it begins to lose water and at about  $150^{\circ}$  C. it becomes anhydrous. At red heat it carbonizes, emitting inflammable gases having a pungent, acrid odor, and leaves a black residue of carbon and sodium carbonate (1).



It is a salt of a strong base and a relatively weak acid and it hydrolyzes sufficiently to impart a slight alkalinity to its aqueous solutions.

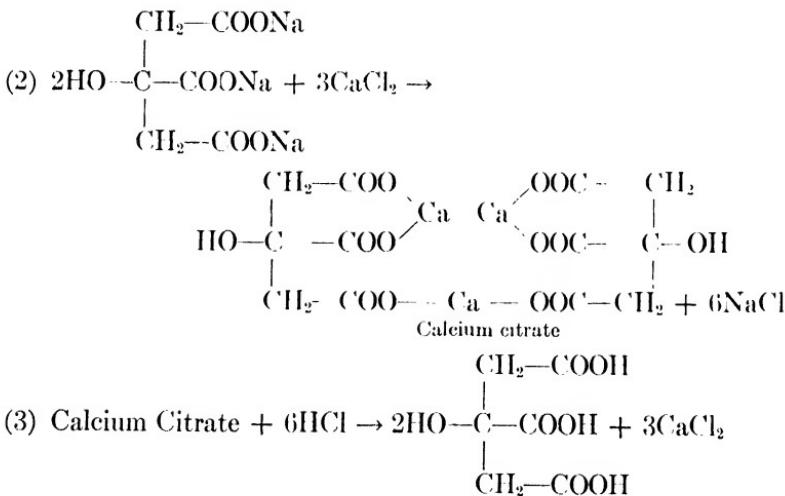
Because sodium citrate in solution ionizes to liberate sodium and citrate ions, the salt may be used as a buffer against acids. The mechanism whereby this takes place is through the citrate ion, which will take up hydrogen (or hydronium) ions from highly ionized acids such as hydrochloric acid, to form relatively non-ionized citric acid. The following schematic diagram shows the reactions taking place.



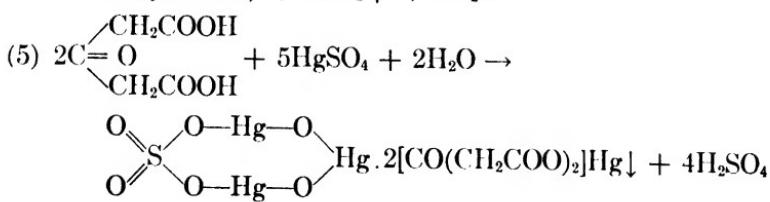
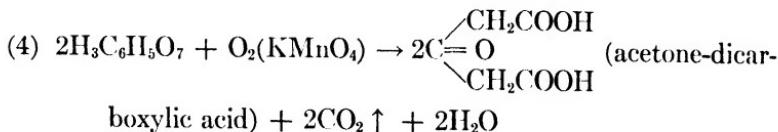
In addition to the official salt which is a dihydrated sodium citrate ( $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ ) there is another common hydrate ( $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 11\text{H}_2\text{O}$ ). This salt also occurs as a well-crystallized compound, 1 Gm. of which is soluble in 1.1 cc. of water at  $25^\circ\text{ C}$ . and 0.4 cc. of water at  $100^\circ\text{ C}$ . It was official in U. S. P. VIII, but was deleted in favor of the more stable dihydrate.

**Official Tests for Identity.**—1. A solution of Sodium Citrate (1 in 20) responds to the tests for *Sodium* (*q. v.*).

2. A 1 in 10 solution also responds to the tests for *Citrate*. (*a*) When an excess of calcium chloride T.S. is added to a cold, neutral solution of sodium citrate, no precipitate is produced. However, when the solution is heated, a white granular precipitate of calcium citrate settles out (2). The precipitate is insoluble in sodium hydroxide T.S., but dissolves immediately in diluted hydrochloric acid (3) due to formation of water-soluble citric acid and calcium chloride.

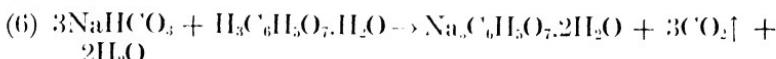


(*b*) If potassium permanganate T.S. is added to a hot solution of sodium citrate, to which has been added one-tenth of its volume of mercuric sulfate T.S. (Denigé's reagent), a white precipitate is produced (4, 5). Tartrates do not give this precipitate. The equations for the reactions thought to take place are given below.



3. When ignited, sodium citrate behaves in the manner characteristic of almost all metallic salts of organic acids, in that it first chars and burns, and then upon continued heating yields a residue of sodium carbonate (1) which effervesces with acids, and imparts the yellow sodium color to a non-luminous flame.

**Commercial Manufacture.**—Sodium citrate is made by neutralizing a solution of citric acid with sodium carbonate or bicarbonate (6). When effervescence has ceased, the solution is evaporated to crystallization or, more frequently, the salt is granulated in the usual way.



**Laboratory Preparation.**—Dissolve 10 Gm. of citric acid in 50 cc. of distilled water contained in an evaporating dish and add small quantities of sodium bicarbonate to the solution until effervescence ceases. Evaporate on a steam bath and granulate in the usual way. (See equation 6.)

**Pharmaceutical Preparations and Uses.**—1. *Sodium Citrate* (Sodii Citras), U. S. P. XIII.—“Sodium Citrate, when dried at 150° C. to constant weight, contains not less than 99 per cent of  $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7$ .” The uses of sodium citrate are considered under the specific headings as follows:

(a) *Orally*, sodium citrate is ingested into the body and is oxidized in the tissues to sodium bicarbonate. This oxidization is not as rapid as that taking place with acetates. Its therapeutic value, orally, depends then on this alkalinization, and hence its use to relieve mild acidosis and also to promote a diuretic effect. (See also Sodium Acetate, p. 150.) A non-official compound which is closely related to sodium citrate is disodium citrate which has an analogous action to and is said to have a more agreeable taste than the official salt.

(b) *Parenterally*, sodium citrate is capable of shortening the coagulation time of the blood, although this seems entirely in contradiction to its anticoagulant action on blood *in vitro*.

(c) *In vitro*, when sodium citrate is added to freshly drawn blood it prevents the coagulation of blood over a relatively long period of time. This action, probably due to the inactivation of blood calcium as undissociated calcium citrate, is utilized in making blood transfusions, wherein the blood is drawn into a flask containing a suitable amount of sodium citrate. The drawn blood may then be kept for some time, or may be used immediately without danger of clotting. The citration of blood is usually carried out by using a 2.5 per cent sodium citrate solution, in the proportion of 10 cc. to 100 cc. of the donor's blood. It is necessary that citrated blood be stored at body temperature and it should be used as soon as possible.

(d) *Pharmaceutically*, sodium citrate is often used to prevent discoloration of various preparations such as the glycerites of phenol

and tannic acid. (See p. 185.) Average dose—1 Gm. (approximately 15 grains).

2. *Penicillin Tablets* (*Tabellæ Penicillini*), U. S. P. XIII.—These tablets contain "penicillin calcium or penicillin sodium buffered with calcium carbonate, anhydrous sodium citrate, aluminum hydroxide, or other buffers, approved by the Federal Food and Drug Administration." Because of the unpleasant features connected with the parenteral administration (intramuscular) of penicillin, investigators were active in trying to find a means of protecting penicillin from the inactivating effects of the acid gastric juices (it is also inactivated by excess alkali). Charney and co-workers<sup>1</sup> used trisodium citrate and disodium citrate as buffer salts to cause formation of the weak acid, citric acid, in the stomach at the expense of the more highly acidic hydrochloric acid normally present in the stomach (see Chemical Properties of Sodium Citrate, p. 181). The better absorption of penicillin was reflected in the raised urinary levels of excreted penicillin. The anhydrous sodium citrate (unofficial) is used to prevent decomposition of the water-sensitive penicillin, inasmuch as the official dihydrate is prone to effloresce and in that way release its water of hydration. Average daily dose of penicillin—on a fasting stomach, 300,000 units.

3. *Anticoagulant Sodium Citrate Solution* (*Liquor Sodii Citratis Anticoagulans*), U. S. P. XIII.—This is a solution of sodium citrate in isotonic solution of sodium chloride and contains, in each 100 cc., not less than 2.3 Gm. and not more than 2.7 Gm. of sodium citrate ( $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ ) and not less than 0.85 Gm. and not more than 0.95 Gm. of sodium chloride (NaCl), including all tolerances.

Three anticoagulant solutions of sodium citrate are designated by the U. S. P. XIII, *viz.*, No. 1—the Non-sterile Solution; No. 2—the Sterile Solution Not for Parenteral Use; and No. 3—the Sterile Solution for Parenteral Use, which is the one that must be dispensed unless otherwise specified.

No. 1 is prepared by dissolving 25 Gm. of Sodium Citrate and 9 Gm. of Sodium Chloride in sufficient distilled water to make 1000 cc. and filtering the solution until it is free from suspended particles.

No. 2 is made as directed for No. 1 but it is sterilized preferably by Process C. (See p. 694, U. S. P. XIII.)

No. 3 is also prepared like No. 1 excepting that the distilled water is replaced by water for injection and, after placing the solution in suitable containers, it is sterilized preferably by Process C. Bacteriostatic agents, of course, must not be added. The pH should not be less than 6.7 and not more than 7.5.

The U. S. P. XIII permits of variations in the sodium citrate content of anticoagulant solutions of sodium citrate, but requires that such solutions must be labeled so as to indicate the per cent or amount of sodium citrate per unit of volume. Such solutions must

<sup>1</sup> Charney *et al.*: *Science*, **101**, 251 (1945).

contain not less than 92 per cent and not more than 108 per cent of the labeled amount of sodium citrate. These solutions must conform to U. S. P. XIII requirements for general methods of preparation, physical properties and tests given for Anticoagulant Sodium Citrate Solution.

4. *Anticoagulant Acid Citrate Dextrose Solution* (*Liquor Acidi Citratis Dextrosi Anticoagulans, A.C.D. Solution*), U. S. P. XIII.—This is "a sterile solution of sodium citrate, citric acid, and dextrose. It contains, in each 100 cc., not less than 2 Gm. and not more than 2.4 Gm. of  $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ , and not less than 750 mg. and not more than 850 mg. of  $\text{H}_3\text{C}_6\text{H}_5\text{O}_7 \cdot \text{H}_2\text{O}$ ." This solution is used in the same manner as Anticoagulant Sodium Citrate Solution, *viz.*, as an anticoagulant for use in preparing plasma or whole blood for indirect transfusions.

5. *Tannic Acid Glycerite* (*Glyceritum Acidi Tannici, Glycerite of Tannin*), U. S. P. XIII.—Tannic Acid Glycerite contains 1 per cent of sodium citrate in addition to the other constituents. It is used in this preparation to prevent discoloration due to the formation of iron tannate. This pharmaceutical is used as an astringent,

6. *Ferric Citrochloride Tincture* (*Tinctura Ferri Citrochloridi*), N. F. VIII.—This tincture requires the use of 450 Gm. of sodium citrate in the preparation of 1000 cc. of finished product. The sodium citrate is added to the preparation to prevent the ferric ion from being precipitated as dark-colored, insoluble iron tannate which constitutes one of the common incompatibilities of iron solutions when mixed with tannin-containing preparations. (See also p. 619.) Average dose—0.5 cc. (approximately 8 minims).

7. *Gentian Elixir* (*Elixir Gentianae*), N. F. VIII.—Gentian Elixir contains 3 per cent of sodium citrate. This preparation is a hydro-alcoholic solution of fluidextract of gentian, sodium citrate, compound cardamom spirit, syrup and glycerin. The sodium citrate prevents the precipitation of iron tannate when the elixir is used as a vehicle for iron salts or solutions.

8. *Compound Hypophosphites Syrup* (*Syrupus Hypophosphitum Compositus*), N. F. VIII.—This preparation contains 0.37 per cent of sodium citrate. The sodium citrate is probably used for solubility purposes. (See p. 622.) Average dose—8 cc. (approximately 2 fluidrachms).

9. *Peptonized Iron* (*Ferrum Peptonatum, Iron Peptone*), N. F. VIII.—"Peptonized Iron is a compound of iron oxide and peptone, rendered soluble by the presence of sodium citrate, and yields not less than 16 per cent and not more than 18 per cent of Fe."

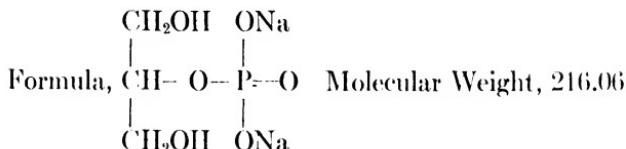
10. *Phenol Glycerite* (*Glyceritum Phenolis, Carbolic Acid Glycerite*), N. F. VIII.—This glycerite contains 1 per cent of sodium citrate to prevent discoloration of the preparation. The glycerite is used for its antiseptic (phenol) and dehydrating (glycerin) action.

11. *Sodium Citrate Solution* (*Liquor Sodii Citratis, Potio Riverii*), N. F. VIII.—This solution "contains, in each 100 cc., not less than 2.5 Gm. and not more than 3 Gm. of  $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ ." The

sodium citrate is prepared by interaction of sodium bicarbonate with citric acid. The citric acid is dissolved in distilled water and the sodium bicarbonate dissolved in this solution with gentle agitation, the bottle being stoppered immediately. It should not be dispensed unless recently prepared.

### SODIUM GLYCEROPHOSPHATE

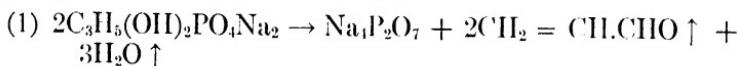
*Sodium Glycerophosphate*, N. F. VIII



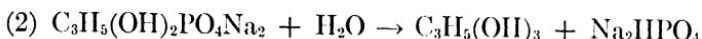
**Physical Properties.**—Sodium Glycerophosphate occurs as white, monoclinic plates or scales, or as a white powder. It is odorless, and has a saline taste. At 15° C. large crystals of the salt are stable in air. When in the form of small crystals or a powder, the salt effloresces slightly in air.

One Gm. of the salt is soluble in about 1.5 cc. of water at 25° C. It is very soluble in hot water, but nearly insoluble in alcohol.

**Chemical Properties.**—When sodium glycerophosphate is strongly heated, it decomposes and at red heat is converted into sodium pyrophosphate, acrolein, and water (1).

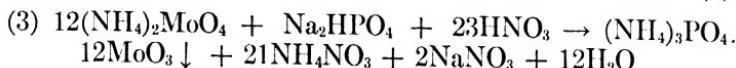


Prolonged boiling of sodium glycerophosphate solutions will bring about hydrolysis of the compound (2).

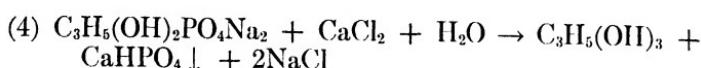


**Official Tests for Identity.**—1. A 1 in 20 aqueous solution of the salt will give all of the tests for Sodium (*q. v.*).

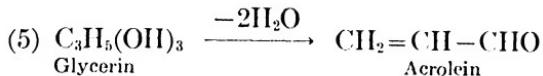
2. Although solutions of glycerophosphates do not yield a precipitate in the cold with ammonium molybdate T.S., boiling will bring about hydrolysis of the glycerophosphate (2) and the resultant phosphate will then yield a precipitate with the reagent (3).



3. Moderately dilute solutions of glycerophosphates, when treated with calcium chloride T.S., remain unaffected in the cold, but on boiling a precipitate is produced, probably through the same mechanism as cited for the previous test. The equations representing the reactions may be conveniently combined into one equation (4).

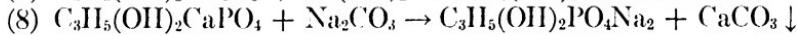
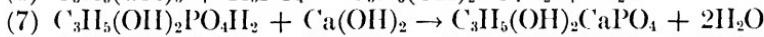
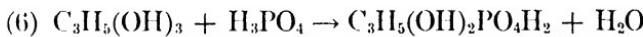


4. When a glycerophosphate is mixed with an equal weight of potassium bisulfate (powdered) and heated, the very pungent odor of acrolein is evolved. The potassium bisulfate, being a dehydrating salt (sometimes regarded as an equimolecular mixture of potassium sulfate and sulfuric acid) will dehydrate the glycerin resulting from the breakdown of the glycerophosphate to yield acrolein (5).



5. When sodium glycerophosphate is strongly heated it decomposes yielding inflammable vapors (1).

**Commercial Manufacture.**—The details of the process used for manufacturing sodium glycerophosphate are not published, hence only a general outline of the method can be given. When glacial phosphoric acid (*q. v.*) is gradually dissolved in an equal weight of glycerin and the resulting solution heated for several hours at 110° C., glycerophosphoric acid is formed (6). This easily decomposable acid is dissolved in cold water, neutralized with milk of lime (7), and the calcium phosphate filtered off. The filtrate is freed of any excess calcium hydroxide by passing carbon dioxide through it and the resulting calcium carbonate is filtered off. The solution is concentrated in a vacuum and the calcium glycerophosphate either granulated or precipitated by alcohol, in which it is nearly insoluble. The calcium salt is washed thoroughly with alcohol to free it from adhering glycerin and then dissolved in water. By the addition of sodium carbonate to the solution, calcium carbonate is precipitated and sodium glycerophosphate remains in solution (8). The latter is then precipitated by the addition of alcohol.



**Pharmaceutical Preparations and Uses.**—1. *Sodium Glycerophosphate* (Sodii Glycerophosphas), N. F. VIII.—“Sodium Glycerophosphate contains not less than 68 per cent and not more than 74 per cent of  $\text{Na}_2\text{C}_3\text{H}_5(\text{OH})_2\text{PO}_4$ .” This salt was introduced into medicine as a tonic, particularly for the nerves. However, no evidence has ever been presented to substantiate this claim. In view of the fact that the salt is easily decomposed in the body to glycerin and inorganic phosphate it is reasonable to believe that its action is no greater than that of inorganic phosphate. Average dose—0.25 Gm. (approximately 4 grains).

2. *Calcium and Sodium Glycerophosphates Elixir* (Elixir Calcii et Sodii Glycerophosphatum, Glycerophosphates Elixir), N. F. VIII.—This preparation contains 1.8 per cent of sodium glycerophosphate together with 0.9 per cent of calcium glycerophosphate and other ingredients. It is used as a tonic although, as stated before, its

value is doubtful. Average dose—4 cc. (approximately 1 fluid-drachm).

3. *Compound Glycerophosphates Elixir* (*Elixir Glycerophosphatum Compositum, Compound Glycerophosphates Solution*), N. F. VIII.—Besides other glycerophosphates (Ca, Fe, and Mn), this preparation contains 3.5 per cent of sodium glycerophosphate. This preparation is prescribed by some physicians as a nerve tonic. Average dose—8 cc. (approximately 2 fluidrachms).

## SODIUM HYDROXIDE

### *Sodium Hydroxide, U. S. P. XIII*

Formula, NaOH. Molecular Weight, 40.01

**Physical Properties.**—Sodium Hydroxide is obtainable in dry, hard, brittle, white or nearly white sticks, in fused masses, in small pellets, in flakes, and in other forms; all having a dense crystalline fracture and a specific gravity of 2.13. It is very deliquescent and rapidly absorbs moisture and carbon dioxide from the air. Sodium hydroxide and its solutions rapidly destroy organic tissues, hence great care is necessary in handling them.

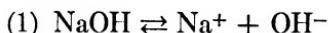
In the cold (0° C. or below), concentrated solutions deposit various crystalline hydrates, whose compositions vary from  $\text{NaOII} \cdot \text{H}_2\text{O}$  to  $\text{NaOH} \cdot 7\text{H}_2\text{O}$ .

Sodium hydroxide melts at 318° C. and volatilizes at higher temperatures. The vapors decompose between 1200° and 1250° C.

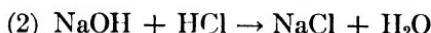
One Gm. of Sodium Hydroxide dissolves in 1 cc. of water at 25° C. with the evolution of heat. One Gm. is soluble in 0.3 cc. of boiling water. It is soluble in alcohol, in ether, and in glycerin.

**Chemical Properties.**—The chemical properties of sodium hydroxide are quite varied and although there is some overlapping it is considered advantageous to discuss them under the headings: (a) basic properties, (b) reaction with salts, (c) reaction with metals, (d) reaction with non-metals, and (e) saponifying properties.

(a) Because sodium hydroxide is so highly ionized when dissolved in water, it is one of the strongest bases (1). As has been previously pointed out, the basic properties are entirely due to the hydroxide ion (see p. 34).



Its excellent acid-neutralizing powers (2) are made use of in various ways, especially in alkalimetry and acidimetry.



The marked ability of sodium hydroxide (as well as many other metallic hydroxides) to absorb  $\text{CO}_2$  with the subsequent formation of the corresponding carbonate is well known. This is a good example of its acid-neutralizing effect. One may consider that

$\text{CO}_2$  on dissolving in water forms carbonic acid (3), which in turn reacts readily with sodium hydroxide to form sodium carbonate (4).

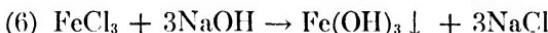


(b) Sodium hydroxide reacts with the salts of all metals in solution, precipitating practically all except those of the alkali metals and ammonium.

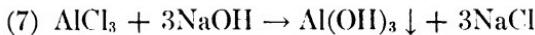
In the case of ammonium salts the product of the reaction is  $\text{NH}_4\text{OH}$  (5). This reaction is used as a test for ammonium ion and is carried out by heating the alkalized solution. The evolution of ammonia (detected by odor or moistened red litmus) is a positive test for presence of ammonium ion.



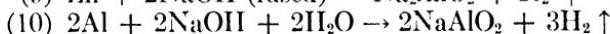
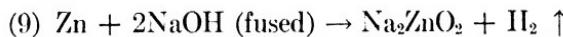
When non-volatile hydroxides are formed they precipitate from solution, as in the case of ferric hydroxide (6).



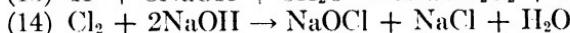
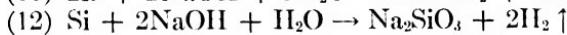
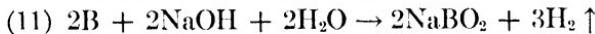
In some cases, an excess of sodium hydroxide will redissolve the precipitated hydroxide. For example, aluminum hydroxide when freshly precipitated (7) will readily dissolve (8) in an excess of sodium hydroxide.



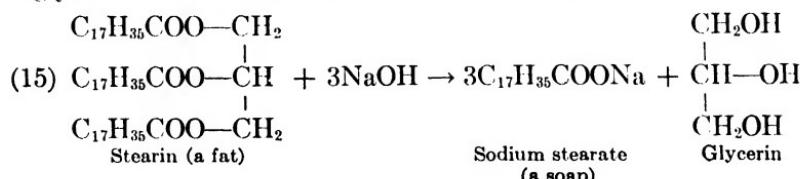
(c) Many metals are attacked either by aqueous solution of sodium hydroxide or by the fused material. Zinc (9) and aluminum (10) are typical examples of metals which react rather easily in this manner.



(d) Among the non-metals which react with sodium hydroxide are boron (11), silicon (12), phosphorus (13), and chlorine (14).



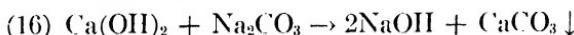
(e) Sodium hydroxide is used extensively because of its very effective saponifying power. (See also Sodium Carbonate, p. 169.) As previously pointed out, saponification of a fat or oil is the process of hydrolyzing it by means of an alkali, *e. g.*, sodium hydroxide (15) to glycerin and the sodium salt of the fatty acids.



**Official Test for Identity.**—A solution of sodium hydroxide (1 in 25) responds to the tests for *Sodium* (*q. v.*).

**Commercial Manufacture.**—Sodium hydroxide, or caustic soda as it is more commonly known, is prepared commercially by either (1) the *chemical* method or (2) the *electrolytic* method. Approximately one-half of the caustic soda manufactured today is made by the chemical process and one-half by the electrolytic method. However, the electrolytic procedure has been gaining in popularity and if the present trend continues will in a large measure replace the chemical method.

1. The chemical method involves causticizing milk of lime. Essentially, the process requires the interaction of sodium carbonate with calcium hydroxide to give sodium hydroxide and insoluble calcium carbonate (16).



The calcium hydroxide is obtained by "slaking" lime ( $\text{CaO}$ ), *i. e.*, adding enough water to the lime to convert it to a dry calcium hydroxide (17).



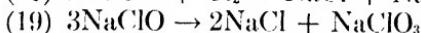
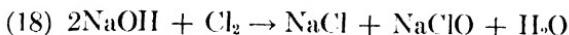
In practice, the dry slaked lime and soda ash (anhydrous  $\text{Na}_2\text{CO}_3$ ) are stirred into water in which they react to form a caustic soda solution containing a suspension of insoluble calcium carbonate. The caustic soda liquor is obtained from this mixture by allowing the precipitate to settle and then decanting the clear liquid. Since the "mud" of calcium carbonate which has settled out has too much caustic soda adhering to it, it is washed and the washings used as the liquid to which slaked lime and soda ash are added. The caustic soda solution obtained by decantation is evaporated either to a 50 per cent solution in which form one-third to one-half of all caustic soda is sold and used, or it may be evaporated in iron pots to the solid form in which case it is obtained as a solid mass which may be crushed or made into flakes. If desired, the fused material may be cast in silver molds into the form of sticks or pellets, the latter being the usual form in which the pharmacist obtains it. The manner in which the small pellets are made is quite interesting. They are made in one of two ways: (1) by dropping the fused material in the same manner as "drop shot" is made, in which case the fused caustic flattens out into a hemisphere when it strikes the receiving plate; (2) by the use of depression plates, in which the fused material is poured on a plate provided with small hemispherical depressions and the excess scraped off. In this case, also, the material is obtained as small hemispheres. The purpose in shaping it into pellets or sticks is to offer a comparatively small surface to atmospheric moisture and  $\text{CO}_2$ , thus minimizing caking, deliquescence and conversion of the product into sodium carbonate.

2. The electrolytic process has already been discussed in some detail (see p. 85) in connection with the manufacture of chlorine.

However, it should be pointed out that two distinct types of electrolytic cells are used, *viz.*, (a) the diaphragm cell, and (b) the mercury cell.

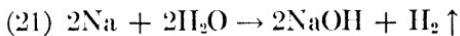
(a) The diaphragm cells are so named because they have the anode and cathode separated by an asbestos diaphragm. Usually the anode is enclosed with a diaphragm. The purpose of the diaphragm is to prevent, insofar as possible, the interaction of sodium hydroxide (around cathode) and chlorine (evolved at anode).

If the products of electrolysis are not separated by a diaphragm the following reactions take place (18, 19, 20):



The cell liquor after electrolysis contains from 8 to 12 per cent of sodium hydroxide and about 15 per cent of sodium chloride. It is concentrated to 50 per cent NaOH in multiple-effect evaporators when most of the sodium chloride crystallizes out of solution. The caustic liquor is then handled in a manner analogous to that cited for the chemical process.

(b) The mercury cell differs radically from the diaphragm cell. In this type of cell mercury is used as a cathode and graphite as the anode. Metallic sodium is the primary cathode product (in contrast to the diaphragm cells) and is deposited on the mercury to form an amalgam. The amalgam (liquid) is conducted into a decomposition cell where it is made to react with water (21) to form sodium hydroxide and hydrogen. The amount of water used is such that a 50 per cent caustic soda solution is obtained, thus obviating the necessity of costly evaporation, which is one of the principal disadvantages of the diaphragm cell.



There are numerous mercury cells described in the literature but apparently the ones in current use have not been accurately described.

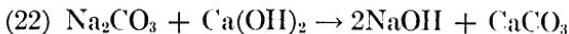
**Pharmaceutical Preparations and Uses.**—1. *Sodium Hydroxide* (*Sodii Hydroxidum, Caustic Soda*), U. S. P. XIII.—“Sodium hydroxide contains not less than 95 per cent of total alkali calculated as NaOH, of which not more than 3 per cent is Na<sub>2</sub>CO<sub>3</sub>.<sup>1</sup>” Sodium hydroxide is so caustic that it finds little use in therapy. However, it is used to some extent in the preparation of various pharmaceuticals. Much of the caustic soda produced commercially is used in the soap industry and also in numerous other ways.

2. *Saponated Cresol Solution* (*Liquor Cresolis Saponatus, Compound Cresol Solution*), U. S. P. XIII.—This solution consists essentially of cresol dissolved in a soap, the soap being formed by the saponification (see p. 189) of any of several oils (corn, linseed, cotton-seed, etc.) with potassium or sodium hydroxide. The official formula calls for potassium hydroxide, but permission is given to use

sodium hydroxide in an equivalent amount if desired. In the event that a different strength alkali is used than that specified, an equivalent amount is to be calculated and used. This preparation is similar to the commercial preparation "Lysol." It is used as a general disinfectant.

3. *Phenolsulfonphthalein Injection* (*Injectio Phenolsulfonphthaleini*), U. S. P. XIII.—This injection has been described previously under Sodium Bicarbonate (see p. 156). The purpose of the sodium hydroxide is the same as that of sodium bicarbonate, namely, to convert the insoluble phenolsulfonphthalein to its water-soluble sodium salt.

4. *Soda Lime* (*Calx Soda*), U. S. P. XIII.—"Soda Lime is a mixture of calcium hydroxide with sodium or potassium hydroxide or both, intended for use in metabolism tests, anesthesia, and oxygen therapy." The U. S. P. states that it may contain an indicator which will not react with the common anesthetic gases, and which will change color when the absorption capacity of the soda lime for CO<sub>2</sub> is exhausted. The function of Soda Lime in a closed system (such as exists in metabolism tests, etc.) is to absorb the CO<sub>2</sub> which otherwise would accumulate in the system. The manner in which this takes place is quite interesting in that it may be interpreted as a case of two chemicals helping one another out for their mutual benefit. In this case, the sodium hydroxide is capable of picking up carbon dioxide with avidity (3, 4), but its combining power is soon exhausted. However, at this point the calcium hydroxide appropriates the accumulated carbon dioxide (22) to form calcium carbonate and thereby relieves the sodium hydroxide. Thus we see a continuous cycle in which the sodium hydroxide is converted to sodium carbonate, but is then changed back to sodium hydroxide which is again capable of combining with CO<sub>2</sub>.



In hospitals, where the uncolored (*i. e.*, with no indicator) form of soda lime is used, it is customary to keep a record of the length of time that a charge of soda lime has been used. From past experience it is then possible to change the soda lime before its strength is exhausted. In the case of soda lime to which has been added an indicator, the color change of the indicator serves warning that it must be changed.

5. *Nitromersol Solution* (*Liquor Nitromersolis*), N. F. VIII.—This solution has been described previously (see p. 172). The sodium hydroxide together with sodium carbonate acts merely as a solubilizing agent for the water-insoluble nitromersol.

6. *Nitromersol Tincture* (*Tinctura Nitromersolis*), N. F. VIII.—This tincture employs 0.1 per cent of sodium hydroxide to aid in keeping the nitromersol in solution. It is used as an antiseptic.

7. *Rectified Turpentine Oil* (*Oleum Terebinthinae Rectificatum*), N. F. VIII.—To prepare Rectified Turpentine Oil from Turpentine

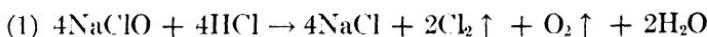
Oil, equal quantities of the oil to be rectified and a solution of sodium hydroxide, containing 5.3 Gm. of 95 per cent NaOH in each 100 cc., are mixed and placed in a still. Upon recovery of three-fourths of the oil by distillation, the clear oil is separated from the water which also comes over and is dried with anhydrous  $\text{CaCl}_2$  or anhydrous sodium sulfate. The use of sodium hydroxide in this preparation is said to bring about the removal of the substances which give a disagreeable odor and taste to the oil. This is probably due to polymerization of aldehydes, saponification of resins, etc., by the alkali. Average dose—0.3 cc. (approximately 5 minims).

### SODIUM HYPOCHLORITE

Formula,  $\text{NaClO}$ . Molecular Weight, 74.45

**Physical Properties.**—Sodium hypochlorite, like all of the hypochlorites, is very unstable and therefore is not obtainable in solid form. It is official only in the form of its solutions.

**Chemical Properties.**—In solution, sodium hypochlorite is decomposed by boiling and by nearly all acids (1).



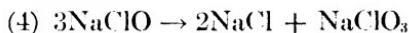
It is a very powerful oxidizing agent; this action being attributable to active oxygen formed upon decomposition (2). Some investigators, however, claim it acts as free chlorine.



A solution of sodium hypochlorite will form a precipitate of silver chloride with solutions of silver nitrate (3).



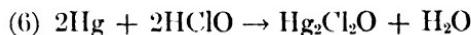
Sodium hypochlorite is readily changed, when warmed, to sodium chloride and sodium chlorate (4). This property is characteristic of all hypochlorites.



Sodium hypochlorite solutions will cause the formation of mercuric oxide and sodium chloride when shaken with metallic mercury (5).



This is in contrast to free hypochlorous acid which reacts to form a brown basic mercuric chloride with metallic mercury (6).



Solutions of potassium iodide liberate free iodine when treated with sodium hypochlorite (7).



**Official Tests for Identity.**—There are no official tests for sodium hypochlorite since it is a non-existent compound *per se*, but the tests given for the Sodium Hypochlorite Solution may be taken as a criterion for the compound itself.

1. The solution at first colors red litmus blue, and then decolorizes it. The blue coloration of the litmus is, of course, due to the fact that sodium hypochlorite is somewhat hydrolyzed in solution and thus exhibits an alkaline reaction. The paper is bleached because of the oxidizing action of the solution.

2. The addition of diluted hydrochloric acid to sodium hypochlorite solution causes an evolution of chlorine (1).

3. The solution obtained in the above experiment responds to the flame test for sodium.

**Commercial Manufacture.**—Most of the commercial products containing sodium hypochlorite are made by electrolyzing a solution of sodium chloride (see p. 191). The cells do not contain a diaphragm and hence the chlorine liberated at the anode contacts the sodium hydroxide produced around the cathode to form sodium hypochlorite. The cell contents are usually cooled with cold water circulated in specially constructed hard rubber tubing, as any marked rise in the temperature is conducive to undesirable sodium chlorate formation.

**Pharmaceutical Preparations and Uses.**—1. *Sodium Hypochlorite Solution* (Liquor Sodii Hypochloritis), U. S. P. XIII.—“Sodium Hypochlorite Solution contains not less than 4 per cent and not more than 6 per cent of NaOCl.” The U. S. P. cautions that this solution is not suitable for application to wounds. It is a clear, pale, greenish-yellow liquid having an odor of chlorine, and it is affected adversely by light. If “*Labarraque’s Solution*” is desired, this solution diluted with an equal volume of water may be dispensed. The solution is used as an oxidizing and bleaching agent. It is interesting to note that a 2 per cent solution is being widely used as a laundry bleaching agent, *e. g.*, Hilex, Hy-Lo, etc.

2. *Diluted Sodium Hypochlorite Solution* (Liquor Sodii Hypochloritis Dilutus, Modified Dakin’s Solution, Liquor Soda Chlorinatae Chirurgicalis), N. F. VIII.—This is an “aqueous solution of chlorine compounds of sodium containing, in each 100 cc., not less than 0.45 Gm. and not more than 0.50 Gm. of NaOCl, equivalent to not less than 0.43 Gm. and not more than 0.48 Gm. of available Cl.”

It is prepared by diluting 1000 cc. of Sodium Hypochlorite Solution with 5000 cc. of distilled water, adding 40 cc. of a 5 per cent solution of sodium bicarbonate in cold distilled water, and mixing the solution thoroughly. Twenty cubic centimeters of the mixture are removed, about 20 mg. of powdered phenolphthalein added, and the mixture shaken gently for two minutes. If a red color develops, more of the solution of sodium bicarbonate is added to the original dilution until no red color is produced when other 20-cc. samples of the mixture are tested as directed above. Then the

percentage of sodium hypochlorite in the solution is determined as directed in the assay, and sufficient distilled water added to make the final solution contain 0.48 Gm. of NaOCl in each 100 cc.

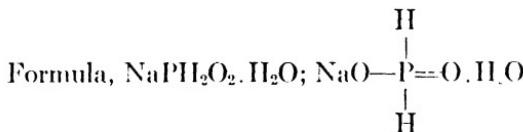
Sodium bicarbonate is a salt composed of a strong base and a weak acid. By the addition of a solution of sodium bicarbonate the  $\text{Na}^+$  is increased and therefore the  $\text{OH}^-$  will be decreased, because the product of the concentrations of the sodium ion and the hydroxide ion divided by the concentration of sodium hydroxide is equal to a constant, *e. g.*,  $\frac{[\text{Na}^+] \times [\text{OH}^-]}{[\text{NaOH}]} = K$ .

The limit of alkalinity is determined by adding about 20 mg. of powdered phenolphthalein to 20 cc. of the solution contained in a test tube. No red color should be produced in the mixture when agitated.

The purpose in buffering this solution is to lower the alkalinity and thus make it more suitable for application to the tissues. It is used as an antiseptic and irrigant for wounds.

### SODIUM HYPOPHOSPHITE

*Sodium Hypophosphite*, N. F. VIII



Molecular Weight, 106.01

**Physical Properties.**—Sodium Hypophosphite occurs in the form of small, colorless, transparent, rectangular plates, having a pearly luster, or as a white granular powder. It is odorless and has a saline taste. The salt deliquesces in moist air.

One Gm. of the salt dissolves in about 1 cc. of water at 25° C., or in about 0.20 cc. of boiling water. It is soluble in alcohol and freely soluble in glycerin at 25° C., and in boiling alcohol. It is slightly soluble in dehydrated alcohol.

**Chemical Properties.**—When sodium hypophosphite is heated, it loses its water of hydration. Upon further heating, it is decomposed into inflammable phosphine (1) ( $\text{PH}_3$ , poisonous), and sodium pyrophosphate is left as a residue (2).



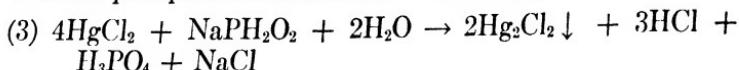
The principal chemical property of hypophosphites is evidenced in their remarkable reducing power. This has already been discussed under Hypophosphorous Acid (p. 115).

**Official Tests for Identity.**—1. It responds to all tests for Sodium (*q. v.*)

2. It responds to all tests for *Hypophosphites*:

(a) When strongly heated, spontaneously inflammable phosphine is evolved (1, 2).

(b) When treated with mercuric chloride T.S., hypophosphites give a white precipitate of mercurous chloride (3).



This precipitate becomes gray with an excess of hypophosphite due to further reduction of the mercurous chloride to free mercury.

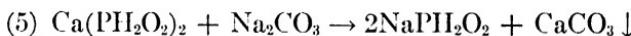
(c) When a solution of sodium hypophosphite is acidified with sulfuric acid and warmed with copper sulfate T.S., a red precipitate of copper hydride is formed. (See p. 115.)

**Commercial Manufacture.**—Sodium hypophosphite is usually prepared by (1) the decomposition of calcium hypophosphite with sodium carbonate, or (2) by the less common method of boiling phosphorus with sodium hydroxide.

1. Calcium hypophosphite is first prepared by the action of phosphorus on milk of lime (4). The products are calcium hypophosphite and phosphine.



Barium hydroxide could be substituted for calcium hydroxide in the above reaction, in which case barium hypophosphite would be formed. The calcium hypophosphite is purified by suitable means (see p. 331) and then reacted with sodium carbonate (5) to yield a precipitate of calcium carbonate together with the sodium hypophosphite which remains in solution. The precipitated calcium carbonate is filtered off and the filtrate carefully evaporated at reduced pressure and with constant stirring until a granular salt is obtained.



2. Sodium hypophosphite may be made by boiling phosphorus with a solution of sodium hydroxide (6). In order to prevent the decomposition of the hypophosphite by any excess alkali, carbon dioxide is passed into the liquid. When the reaction is complete, the solution is carefully evaporated and the sodium hypophosphite dissolved in alcohol, from which it may be granulated or crystallized.



**Pharmaceutical Preparations and Uses.**—1. *Sodium Hypophosphite* (Sodii Hypophosphis), N. F. VIII.—Sodium Hypophosphite, when dried over sulfuric acid for two hours, contains not less than 98 per cent of  $\text{NaH}_2\text{PO}_2 \cdot \text{H}_2\text{O}$ . The N. F. cautions that care should be exercised in compounding sodium hypophosphite with other substances, especially nitrates, chlorates and other oxidizing agents. Because of its marked reducing properties, an explosion may result when it is intimately contacted with oxidizing agents. The use of hypophosphites as nerve tonics has already been shown to be

irrational (see p. 117) because most of them pass through the body unchanged. Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains).

2. *Hypophosphites Syrup* (*Syrupus Hypophosphitum*), N. F. VIII.—This syrup contains 1.8 per cent of sodium hypophosphite together with the same amount of potassium hypophosphite and 3.5 per cent of calcium hypophosphite. The use of this syrup is based on the supposed nerve tonic properties of the hypophosphites. The syrup is probably of little value. Average dose—8 cc. (approximately 2 fluidrachms).

3. *Compound Hypophosphites Syrup* (*Syrupus Hypophosphitum Compositus*), N. F. VIII.—This preparation contains 1.75 per cent of sodium hypophosphite together with other hypophosphites (Ca, K, Fe, and Mn). It is an even more complex preparation than Hypophosphites Syrup but probably has no more value as a nerve tonic. Average dose—8 cc. (approximately 2 fluidrachms).

## SODIUM IODIDE

### *Sodium Iodide*, U. S. P. XIII

Formula, NaI. Molecular Weight, 149.92

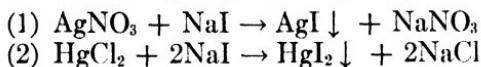
**Physical Properties.**—Sodium Iodide occurs as a white crystalline powder or as colorless, odorless, cubical crystals. The salt cakes and then deliquesces in moist air and frequently decomposes with the liberation of iodine which gives the salt a brown tint. It has a density of 3.667 at 20° C. At temperatures below 30° C., monoclinic crystals with 2 molecules of water separate from aqueous solutions.

One Gm. of Sodium Iodide dissolves in 0.6 cc. of water, in about 2 cc. of alcohol, and in about 1 cc. of glycerin, at 25° C. One Gm. is soluble in 0.4 cc. of boiling water.

Sodium iodide melts at 651° C. At higher temperatures it slowly volatilizes with partial decomposition of the vapors.

**Chemical Properties.**—The chemical reactivity of sodium iodide may be considered from the standpoint of (1) precipitation reactions and (2) ease of oxidation to iodine.

1. Almost all of the iodides are soluble with the exception of silver, mercury (ous and ic), lead, copper (ous), and bismuth. When solutions containing these cations are reacted with solutions of sodium iodide a precipitate of the corresponding insoluble iodide will be formed. For example, silver nitrate precipitates AgI (1), mercuric chloride precipitates HgI<sub>2</sub> (2), etc.



However, in the presence of an excess of sodium iodide (or other soluble iodide) many of the insoluble iodides are converted to soluble compounds (3).



Silver iodide, however, is not solubilized.

2. Sodium iodide (in common with other soluble iodides) is easily oxidized by many reagents to yield iodine.

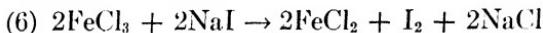
Chlorine water (also bromine water) will displace iodine from its binary compounds as previously shown (see p. 84). Sodium iodide is no exception (4).



Hydrogen peroxide liberates iodine from an acidified (dil.  $\text{H}_2\text{SO}_4$ ) solution of sodium iodide (5).



Ferric salts have sufficient oxidizing power to oxidize sodium iodide to iodine (6), although they are incapable of doing the same to solutions of bromides.



There are numerous other oxidizing agents which are capable of forming iodine from sodium iodide, but the above suffices to illustrate this type of reaction.

**Official Tests for Identity.**--1. The salt responds to all tests for Sodium (*q. v.*).

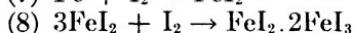
2. Solutions (1 in 20) of sodium iodide respond to all tests for *Iodide*:

(a) The addition of chlorine T.S. causes the liberation of iodine (4) which colors the solution yellow to red. If the iodine is dissolved from the water by shaking the latter with chloroform, the chloroform is colored purple. This free iodine will color starch blue.

(b) The addition of silver nitrate test solution will cause the precipitation of insoluble yellow silver iodide (1) which is insoluble in diluted nitric acid and also in excess ammonia T.S.

**Commercial Manufacture.**--Sodium iodide is manufactured by two processes which are analogous to those described in detail for the laboratory preparation of potassium bromide (*q. v.*). Briefly, these methods involve (1) the decomposition of ferrous iodide with sodium carbonate or (2) the action of iodine upon a solution of sodium hydroxide. (See Sodium Bromide.)

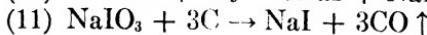
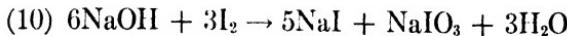
1. Iodine may be reacted with iron wire or filings to obtain ferrous iodide (7, 8) which is then decomposed with sodium carbonate (9).



The ferroso-ferric oxide is filtered out and the filtrate is concentrated to obtain the sodium iodide.

2. As in the analogous case of sodium bromide, iodine may be added to a solution of sodium hydroxide until a slight excess is present. This causes the formation of sodium iodide and sodium

iodate (10). The sodium iodate is converted to iodide by reduction with carbon (11).



**Laboratory Preparation.**—(See Laboratory Method of Preparation for Potassium Iodide, p. 249.)

**Pharmaceutical Preparations and Uses.**—1. *Sodium Iodide* (*Sodi Iodidum*), U. S. P. XIII.—“Sodium Iodide, when dried at 120° to constant weight, contains not less than 99 per cent of NaI.” Therapeutically, sodium iodide has the action of the iodide ion. (See Pharmacology of Iodide Ion, p. 95.) It may be administered orally or intravenously. The intravenous route is said (in commercial literature) to avoid gastric discomfort and to be less likely to produce *iodism*. However, the N. N. R. (1947) gives the following warning, “The intravenous injection of sodium iodide is a dangerous proceeding. While it is tolerated in many cases without bad effects, it may produce not only acute and violent iodism, but also colloidoclastic shock and pulmonary edema. It should therefore not be employed to secure the ordinary actions of iodides, except in very special and restricted conditions, such as (1) certain rare cases of acute thyrotoxicosis with severe vomiting, and (2) in severe paroxysms of asthma.”

In pharmaceutical practice sodium iodide may be used to dissolve difficultly water-soluble substances, *e. g.*, iodine by forming a water-soluble salt (see also KI, p. 248). Average dose—0.3 Gm. (approximately 5 grains).

2. *Iodine Tincture* (*Tinctura Iodi*, Mild Tincture of Iodine, U. S. P. XII), U. S. P. XIII.—Contains 2.1 to 2.6 per cent of sodium iodide. (See p. 96.)

3. *Iodine Solution* (*Liquor Iodi*), N. F. VIII.—This solution contains not less than 2.1 Gm. and not more than 2.6 Gm. of NaI in each 100 cc. as an aid in holding the iodine in solution. Sodium iodide is used instead of potassium iodide because the sodium iodide is said to be better tolerated by the tissues. (See also p. 98.)

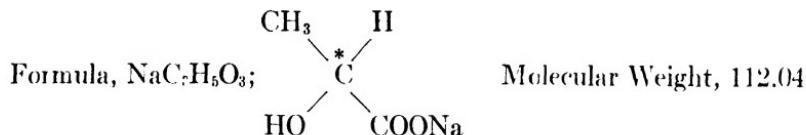
4. *Sodium Iodide Ampuls* (*Ampullæ Sodii Iodidi*, Sodium Iodide Injection), N. F. VIII.—These ampuls “contain a sterile solution of sodium iodide, in water for injection, and yield NaI, equal to not less than 95 per cent and not more than 103 per cent of the labeled amount of NaI.” As pointed out above, the intravenous use of sodium iodide gives rapid iodide action with possible side effects. It is marketed as a 10 or 20 per cent solution usually in 10 or 20 cc. ampuls. Administration of from 10 to 20 cc. of the solution at 2 to 6 day intervals is advocated until results are obtained. Average dose—1 Gm. of Sodium Iodide.

5. *Sodium Salicylate and Iodide Ampuls* (*Ampullæ Sodii Salicylatis et Iodidi*, Sodium Salicylate and Iodide Injection), N. F. VIII.—These ampuls “contain a sterile solution of sodium salicylate and

sodium iodide in water for injection, and yield  $C_6H_4.OH.COONa$ , and  $NaI$ , equal to not less than 93 per cent and not more than 103 per cent of the labeled amount of each." This is a combination which seems to be of especial value in the treatment of rheumatic conditions. One of its advantages lies in the fact that both drugs are administered intravenously and in that manner the gastric discomfort usually attending their oral administration is avoided. The preparation has found some use in the treatment of pneumonia, arthritis, and also asthma. Average dose—1 Gm. of Sodium Salicylate and 1 Gm. of Sodium Iodide.

6. *Sodium Salicylate and Iodide With Colchicine Ampuls* (Ampullæ Sodii Salicylatis et Iodidi cum Colchicina, Sodium Salicylate and Iodide With Colchicine Injection), N. F. VIII.—These ampuls "contain a sterile solution of sodium salicylate, sodium iodide, and colchicine in water for injection, and yield  $C_6H_4.OH.COONa$ , and  $NaI$ , equal to not less than 93 per cent and not more than 103 per cent of the labeled amounts of each." The use of this ampul is similar to the use of Sodium Salicylate and Iodide Ampuls with the added antiarthritic, antirheumatic and analgesic effect of colchicine. Average dose—1 Gm. of Sodium Salicylate, 1 Gm. of Sodium Iodide, and 0.65 mg. of Colchicine.

### SODIUM LACTATE



**Physical Properties.**—Sodium lactate occurs as a colorless or almost colorless, thick, odorless liquid. It is miscible with water and alcohol to give a neutral solution. In commerce it is available in admixture with water containing 70 to 80 per cent of sodium lactate.

**Chemical Properties.**—This salt is easily ignited to form sodium carbonate,  $CO_2$  and water (1).

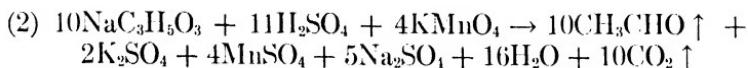


Because of the asymmetric carbon atom (\*) in the lactic acid portion of the molecule there are two recognized forms of sodium lactate, namely sodium *d*-lactate and sodium *l*-lactate. However, the commercial salt is usually a racemic mixture consisting of equal parts of each of the above and may be termed sodium *r*-lactate. The *d*-lactate when administered intravenously is converted almost entirely to liver glycogen. The *l*-lactate is converted into sodium bicarbonate. In this way injection of the *r*-lactate is accompanied by both alkalinization ( $NaHCO_3$ ) and antiketogenic effect (liver glycogen).

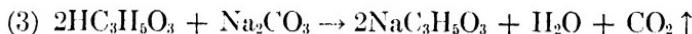
From a knowledge of lactate solubilities, the precipitation reactions of sodium lactate may be readily predicted. The lactates of the alkali metals are very soluble, those of the alkaline earth metals are only slightly soluble (*e. g.*, calcium lactate), and practically all others are insoluble.

**Tests for Identity.**—1. Solutions of sodium lactate respond to all tests for *Sodium* (*q. v.*).

2. When solutions of lactates are acidified with sulfuric acid and then heated with potassium permanganate T.S. they liberate acetaldehyde which may be recognized by its odor (2).



**Commercial Manufacture.**—Sodium lactate is made commercially by neutralizing dilute solutions of lactic acid with either sodium carbonate (3) or sodium hydroxide (4).



The solution resulting from the neutralization is then concentrated to obtain sodium lactate as a 70 to 80 per cent solution.

**Pharmaceutical Preparations and Uses.**—1. *Lactated Ringer's Solution* (Liquor Ringeri Lacticus), U. S. P. XIII.—In addition to sodium chloride, potassium chloride and calcium chloride, this solution contains not less than 290 mg. and not more than 330 mg. of sodium lactate per 100 cc. Its use is discussed on p. 179.

2. *Sodium Lactate Injection* (Injectio Sodii Lactatis), U. S. P. XIII.—“Sodium Laetate Injection is a sterile solution of sodium lactate ( $\text{NaC}_3\text{H}_5\text{O}_3$ ) in water for injection. It contains not less than 95 per cent and not more than 110 per cent of the labeled amount of  $\text{NaC}_3\text{H}_5\text{O}_3$ .” This injection is usually marketed as a 1 molar solution of the racemic form (*r*-lactate) which must be diluted with 5 volumes of sterile distilled water prior to use. The purpose of the dilution is to reduce the concentration to  $\frac{1}{6}$  molar which is approximately isotonic with the body fluids. Injection of sodium lactate may be intravenously, intraperitoneally, or subcutaneously depending on the rapidity with which results are required. The function of sodium lactate, and incidentally the reason it is included in this text, is that the tissues oxidize it very readily to sodium bicarbonate with a resultant systemic alkalinizing effect. The use of sodium lactate as an alkalinizing agent has certain advantages over the use of sodium bicarbonate in that it may be readily sterilized and does not produce a systemic alkalosis as readily as sodium bicarbonate. Furthermore, the salt is anti-ketogenic in that it corresponds to the effect obtained with dextrose solution, *i. e.*, glycogen deposition in the liver. To summarize, it may be said that sodium lactate can be used in all conditions where

the systemic alkalinizing effect of sodium bicarbonate is desired to combat acidosis, *e. g.*, severe dehydration in diarrheas, diabetes mellitus, renal insufficiency, etc.

### SODIUM NITRITE

#### *Sodium Nitrite, U. S. P. XIII*

Formula,  $\text{NaNO}_2$ ;  $\text{NaO}—\text{N}=\text{O}$ . Molecular Weight, 69.01

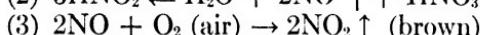
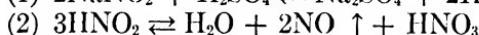
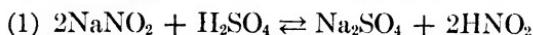
**Physical Properties.**—Sodium Nitrite occurs in the form of (1) white or nearly white, opaque, fused masses or sticks, (2) colorless, transparent, hexagonal crystals, or (3) white or slightly yellow granular powder. It is odorless and has a mild, saline taste. It has a specific gravity of 2.168 at  $20^\circ \text{ C}$ . When exposed to the atmosphere, it deliquesces and is slowly oxidized to sodium nitrate.

One Gm. of Sodium Nitrite dissolves in 1.5 cc. of water at  $25^\circ \text{ C}$ . It is very soluble in boiling water but only sparingly soluble in alcohol.

When heated to  $271^\circ \text{ C}$ . the salt melts, and at red heat it decomposes into oxygen, nitrogen, oxides of nitrogen, and sodium oxide.

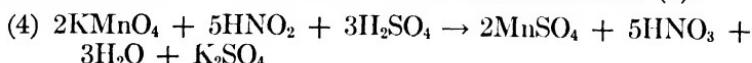
**Chemical Properties.**—Aqueous solutions of sodium nitrite are alkaline because nitrous acid is a weak acid and its salts are appreciably hydrolyzed in solution.

All nitrites are easily decomposed by acidification with dilute sulfuric acid to yield nitric oxide which is readily oxidized by atmospheric oxygen to form  $\text{NO}_2$  (1, 2, 3).

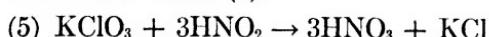


The reactions of the nitrites fall into two categories in which (1) the nitrite acts as a *reducing agent* and (2) the nitrite acts as an *oxidizing agent*.

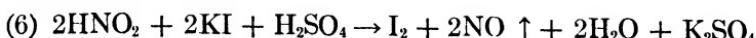
1. When the nitrite acts as a reducing agent it itself is oxidized to the nitrate. Potassium permanganate, for example, is readily reduced when treated with sodium nitrite in acid solution (4).



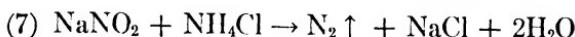
The chlorates (of the alkali metals) are likewise reduced by acidified solutions of the nitrite (5).



2. The oxidizing action of the nitrites is accompanied by formation of nitric oxide ( $\text{NO}$ ) or nitrogen. The oxidation of an acidified (acetic acid or dil.  $\text{H}_2\text{SO}_4$ ) solution of potassium iodide to iodine illustrates the former (6).



The oxidation of ammonium chloride illustrates the latter (7).



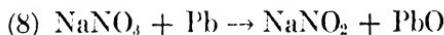
**Official Tests for Identity.**—1. A solution of sodium nitrite responds to the tests for *Sodium* (*q. v.*).

2. A solution of sodium nitrite also responds to the tests for *Nitrite*:

(a) When treated with mineral acids or acetic acid, nitrites yield brownish-red fumes of nitrogen dioxide (1, 2, 3).

(b) A few drops of potassium iodide T.S. added to an acidified solution of a nitrite liberates free iodine which responds to the starch test (turns starch blue) (8).

**Commercial Manufacture.**—1. Sodium nitrate is melted in iron pans and sheet lead added a little at a time (8). The temperature is kept between 450° and 500° C., to prevent the destruction of the iron pan. The fused mass is poured into water and any alkali developed during the reaction is neutralized with diluted sulfuric acid. Lead oxide settles to the bottom of the vat. The aqueous solution of sodium nitrite is sometimes treated with carbon dioxide to remove any dissolved lead, concentrated in open pans to a specific gravity of 1.47, and allowed to crystallize in special vessels. By this process approximately 93 per cent of the sodium nitrate is converted into sodium nitrite. A salt containing 98 per cent of sodium nitrite may be obtained by recrystallizing the product from hot water.



2. Sodium nitrite is also made by mixing a concentrated solution of sodium nitrate with quicklime. The mixture is heated and then air-free sulfur dioxide is passed through it (9). The precipitate is allowed to settle and the supernatant liquor filtered and concentrated to crystallization.



3. When a mixture of sodium nitrate and sodium hydroxide is fused at 300° C. and anhydrous calcium sulfite added, the nitrate is reduced to the nitrite (10).



4. Most of the sodium nitrite is now obtained by absorbing the NO gases, resulting from the catalytic oxidation of ammonia, in NaOH. (See p. 122.)

Frequently, the crystallized sodium nitrite obtained by any one of the above processes is fused and the melt poured into stick or pencil-shaped moulds.

**Laboratory Preparation.**—Fuse 30 Gm. of sodium nitrate in an iron crucible and heat between 450° and 500° C. At this temperature any water of hydration is driven off and iodides and iodates

are decomposed. To the fused mass at 450° C. add 75 Gm. of lead (in thin sheets), in divided portions, stirring constantly (8). Stir the mixture more or less continuously for four hours, and maintain it in the fused condition for three and a half hours longer. Pour this molten mass into water which is constantly agitated.

*Note.*—At this point there is formed about 1 per cent of sodium hydroxide in which lead is soluble. The solution also contains sodium nitrite, sodium chloride and sodium nitrate. The residue consists of lead, lead oxide and lead peroxide.

Strain the residue from the washings, dilute the latter until it has a specific gravity of 1.342, and neutralize with diluted nitric or sulfuric acid. Concentrate the liquid to a specific gravity of about 1.47, clarify by standing, and set it aside in a glass dish to crystallize. Recrystallize the salt from hot water.

**Pharmaceutical Preparations and Uses.**—1. *Sodium Nitrite* (*Sodii Nitris*), U. S. P. XIII.—Sodium Nitrite, when dried over sulfuric acid for four hours, contains not less than 97 per cent of  $\text{NaNO}_2$ . The principal action that can be ascribed to sodium nitrite is that of relaxing smooth muscle, especially that in the smaller blood vessels. This action lowers the blood pressure markedly. Because of this action sodium nitrite has been used in a variety of diseases, of which angina pectoris is of particular importance. It requires from five to twenty minutes to obtain the nitrite effect from a dose of the drug but the activity lasts from one to two and a half hours. Because of its slow onset of action it is without value in the treatment of an acute attack. However, it is a cheap and effective prophylactic drug for use in angina pectoris.

Sodium nitrite has been more or less discredited<sup>1</sup> in the treatment of essential hypertension, its use being termed "illogical and dangerous." The salt is used in the treatment of cyanide poisoning.<sup>2</sup>

Sodium Nitrite has the ability to form methemoglobin when injected into the animal body. Methemoglobin reacts readily with cyanide ion to form cyanmethemoglobin in which form the cyanide ion is incapable of exerting its toxic effects. Sodium thiosulfate is injected following the nitrite, in order to convert the cyanide to the much less toxic thiocyanate. Average dose—60 mg. (approximately 1 grain).

2. *Sodium Nitrite Tablets* (*Tabellæ Soda Nitritis*), U. S. P. XIII.—These tablets "contain not less than 93 per cent and not more than 107 per cent of the labeled amount of  $\text{NaNO}_2$ ." These tablets offer a convenient method of administration of sodium nitrite, since solutions of sodium nitrite are unstable.

3. *Copaiba Mixture* (*Mistura Copaiæ, Lafayette Mixture*), N. F. VIII.—Copaiba Mixture contains 0.3 per cent of sodium nitrite in addition to numerous other ingredients. This preparation was originally introduced as a gonorrhea remedy, but finally

<sup>1</sup> Weiss and Ellis: *Arch. Int. Med.*, **52**, 105 (1933).

<sup>2</sup> Chen, Rose, and Clowes: *Am. J. Med. Sci.*, **188**, 767 (1934). See also Goodman and Gilman: *Pharmacological Basis of Therapeutics*, The Macmillan Company p 701 (1941).

came to be used for its diuretic action. This preparation is outdated and has been superseded by many superior drugs. (See Potassium Hydroxide, p. 246.) Average dose—8 cc. (approximately 2 fluidrachms.)

### SODIUM PERBORATE

#### *Sodium Perborate, U. S. P. XIII*

Formula,  $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ . Molecular Weight, 153.88

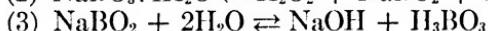
**Physical Properties.**—Sodium Perborate occurs as white, crystalline granules or as a white powder. It crystallizes in transparent, colorless, monoclinic prisms. It is odorless and has a saline taste. The salt is stable in cool, dry air free from carbon dioxide. In warm ( $40^\circ \text{ C.}$ ) or in moist air, it is decomposed with the evolution of oxygen. One Gm. is soluble in about 40 cc. of water.

**Chemical Properties.**—Sodium perborate in aqueous solution slowly hydrolyzes at room temperature to form sodium metaborate and hydrogen dioxide (1) from which oxygen is slowly evolved. When the solution is warmed to  $40^\circ \text{ C.}$ , the oxygen is given off more rapidly.



Some investigators claim that the official formula does not accurately represent the constitution of this compound and contend that  $\text{NaBO}_2 \cdot \text{H}_2\text{O}_2 \cdot 3\text{H}_2\text{O}$  is the correct composition. This would explain the ease with which it is hydrolyzed yielding  $\text{H}_2\text{O}_2$  (1).

Solutions of the salt are alkaline in reaction. This is readily explained on the basis of its hydrolysis equations (2, 3).



The reactions of sodium perborate may be summarized as being a composite of those involving the sodium ion, hydroxide ion, boric acid, hydrogen peroxide and metaborate ion, all of which have been discussed previously.

**Official Tests for Identity.**—1. An aqueous solution gives an alkaline reaction to both litmus and phenolphthalein (2, 3).

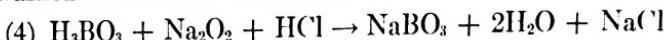
2. The salt in solution gives the same test with turmeric paper as is obtained with borates (see p. 101).

3. Because hydrogen peroxide is obtained by the hydrolysis of the salt (1), the test for hydrogen peroxide (see p. 57) is used to detect the salt. This test is carried out by agitating a mixture of 1 cc. of an aqueous solution of the salt (1 in 50), 1 cc. of diluted sulfuric acid, a few drops of potassium dichromate T.S. and 2 cc. of ether. A blue color in the ether constitutes a positive test.

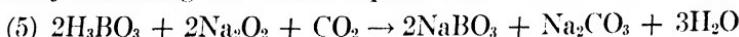
**Commercial Manufacture.**—Two of the methods used for the manufacture of sodium perborate are of German origin and differ only in the conditions under which boric acid and sodium peroxide react to form the salt.

1. Jaubert's method involves the mixing of boric acid and sodium

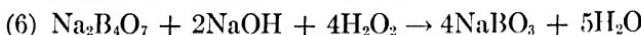
peroxide and slowly adding it to cold water acidulated with either sulfuric or hydrochloric acids (4). The crystals that separate out are washed with alcohol and dried at 58° C.



2. Another method which is said to yield better results is to add 150 kilos of sodium peroxide to 200 liters of cold water. A rise in temperature is prevented by the addition of ice. One hundred and fifty kilos of boric acid are then added and carbon dioxide passed into the liquid until 50 cc. of the filtered solution only reduces the permanganate in 5 to 10 cc. of an acidulated ( $\text{H}_2\text{SO}_4$ ) fifth-normal solution of potassium permanganate. The reaction mixture is kept cold during the entire operation and the reaction is finally completed by saturating the mother liquors with sodium chloride (5).



3. Sodium perborate may be prepared by adding sodium hydroxide and twice the theoretical quantity of hydrogen dioxide to a saturated aqueous solution of borax (6).

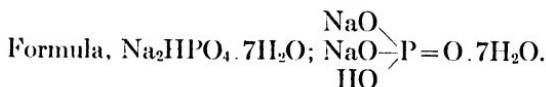


**Pharmaceutical Preparations and Uses.**—1. *Sodium Perborate* (Sodii Perboras), U. S. P. XIII.—“Sodium Perborate contains not less than 9 per cent of available oxygen, corresponding to about 86.5 per cent of  $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ . ” The use of this salt depends entirely upon its ability to form hydrogen peroxide upon hydrolysis (essentially nascent oxygen). Because of this formation of hydrogen peroxide it has been used orally a great deal in the treatment of Vincent’s angina. In this disease (commonly known as “trench mouth”) sodium perborate is applied as a glycerin or water paste, and this may be supplemented by using a 2 per cent (saturated) solution as a mouth wash. It is widely used as a dentifrice, although there is some danger of corrosion due to lodging of particles in the teeth with resultant hydrolysis (2, 3) to sodium hydroxide. It is occasionally used as a dusting powder.

2. *N. F. Aromatic Sodium Perborate* (Sodii Perboras Aromaticus, N. F.), N. F. VIII.—This preparation consists simply of sodium perborate which has been pleasantly flavored with 4 cc. of peppermint oil and 4 Gm. of Saccharin Sodium per 1000 Gm. of preparation. The flavoring covers the saline taste and makes it a better preparation for oral use.

### SODIUM PHOSPHATE

*Sodium Phosphate*, U. S. P. XIII



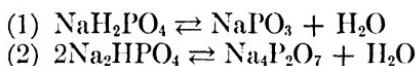
Molecular Weight, 268.09

**Physical Properties.**—Disodium hydrogen phosphate crystallizes from cold solutions in large, colorless, odorless, monoclinic prisms

having 12 molecules of water of hydration. It also occurs as a colorless or white granular salt. It has a not unpleasant saline taste. The salt has a specific gravity of 1.524 at 16° C. and easily effloresces in air, losing 5 molecules of water. When crystallized from solutions above 35° C., it contains 7 molecules of water. This hydrate is the official form of the salt. It effloresces in warm, dry air.

One Gm. of Sodium Phosphate dissolves in 4 cc. of water at 25° C. It is very slightly soluble in alcohol.

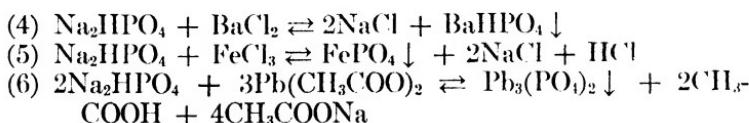
**Chemical Properties.**—When the salt is heated to 40° C., it fuses to a colorless liquid. At 100° C. it becomes anhydrous and at about 300° C. it is converted into sodium pyrophosphate (2). It may be noted that when either the primary or secondary sodium phosphates are heated they lose water and are converted into sodium metaphosphate in the former instance (1) and into sodium pyrophosphate in the latter (2). Tertiary sodium phosphate is unchanged by heating because it does not contain any of the original hydrogen of orthophosphoric acid.



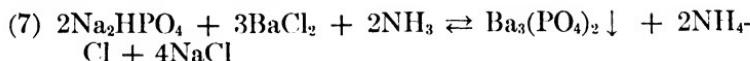
An aqueous solution of disodium hydrogen phosphate is alkaline to litmus paper and to phenolphthalein test solution. As previously stated (p. 126), this is occasioned by hydrolysis, *i. e.*, the tendency of the hydrogen ion of the water to combine with the monohydrogen phosphate ion to form dihydrogen phosphate ion. The alkalinity, of course, is due to the presence of hydroxide ion (3).



Much of the chemistry of the phosphate ion has already been discussed (see p. 126), but it should be pointed out again that many of the incompatibilities of this salt which are not due to its alkalinity, are due to insoluble salt formation. Insoluble salts are readily formed with silver salts, barium salts (4), ferric salts (5), and lead salts (6).

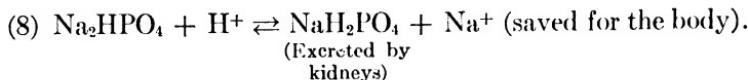


In reaction (4) the presence of ammonia will cause the formation of tertiary barium phosphate (7).



In addition to the sodium bicarbonate:carbonic acid buffer system in the body, we also have a phosphate buffer system which is composed of  $\text{NaH}_2\text{PO}_4$  and  $\text{Na}_2\text{HPO}_4$ . This system, while not as important as the  $\text{NaHCO}_3:\text{H}_2\text{CO}_3$  system, still plays an important

rôle in the regulation of body pH. It is especially adapted to taking care of acidic substances and, although slow, it is probably the most efficient because it guards the alkali reserve. The probable mechanism is by transformation of disodium phosphate by the kidney to the monosodium form with the consequent saving of 1 mole of alkali for the body (8).



Phosphorus-containing foods, which are oxidized in the tissues to orthophosphoric acid, are probably the origin of disodium phosphate. It is said that this buffer system is composed of 80 per cent of the disodium salt and the remainder the monosodium salt.

**Official Tests for Identity.**—Aside from the fact that aqueous solutions of this salt are alkaline to phenolphthalein, its tests are exactly the same as those given for Sodium Biphosphate (p. 160).

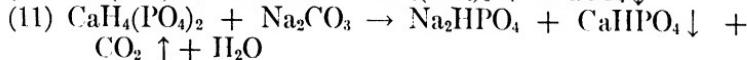
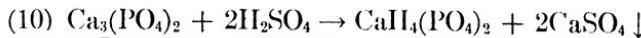
**Commercial Manufacture.**—Disodium hydrogen phosphate is manufactured by (1) neutralizing orthophosphoric acid with sodium carbonate and (2) from bone ash or phosphorite (*q. v.*).

1. Sodium carbonate does not affect the third hydrogen in phosphoric acid and, therefore, the result of interaction is disodium hydrogen phosphate (9).



The solution containing the salt is concentrated to crystallization at a specified temperature (see Physical Properties) to obtain either heptahydrate or the hydrate containing 12 moles of water. The crystals are centrifuged, washed and dried. Care is taken to prevent efflorescence of the salt.

2. The salt is also prepared by first digesting bone ash or phosphorite for several days with diluted sulfuric acid (10). The resulting solution of phosphoric acid and primary calcium phosphate is then concentrated in order to completely separate the calcium sulfate, filtered, diluted, and sodium carbonate added until precipitation ceases (11). The filtered solution is concentrated and allowed to crystallize.



**Pharmaceutical Preparations and Uses.**—1. *Sodium Phosphate* (Sodii Phosphas, Dibasic Sodium Phosphate, Disodium Orthophosphate, Disodium Hydrogen Phosphate), U. S. P. XIII.—“Sodium Phosphate, when dried to constant weight at 110°, contains not less than 98 per cent of  $\text{Na}_2\text{HPO}_4$ .” This salt (the first phosphate salt commercially prepared) is used principally for its laxative properties. The administration of 2 to 4 Gm. of sodium

phosphate in a glass of hot water an hour before breakfast usually results in a single soft stool within an hour. It belongs to a class of laxatives known as "saline laxatives." There are many schemes of classification of laxatives, but the one adopted by Green<sup>1</sup> is easily understood. He divides the laxatives in the following way:

A. BULK-INCREASING LAXATIVES:

1. Cellulose and non-digestible polysaccharides (mucilages).
2. Saline cathartics.
3. Liquid petrolatum.

B. IRRITANT CATHARTICS:

1. Vegetable acids and sulfur.
2. Castor oil.
3. Anthraquinone cathartics and phenolphthalein.
4. Drastic purgatives.
5. Mercurial purgatives.

About *saline laxatives* he says "If a hypertonic solution of sodium chloride is in contact with the intestine it does not remain hypertonic long. The intestine, being permeable to both sodium ions and chloride ions, soon absorbs enough of the salt to render the solution isotonic and no purging takes place. If a solution of sodium sulfate is placed in the gut, a different condition exists. The intestine is permeable to sodium ions but not to sulfate ions. The sulfate ions (and enough positive ions to balance it) stay behind creating a hypertonic state. This can be alleviated only by the introduction of water from the blood and other tissues until the fluid inside the intestine is again isotonic. The increased pressure of this extra water, by virtue of its bulk, brings about catharsis. This is what happens when the physician prescribes a saline cathartic during edema; the water from the edematous area enters the gut to render its contents isotonic."

Any simple inorganic compound can behave as a saline cathartic providing the intestine is impermeable to one or more of its ions. Compounds like magnesium sulfate, in which neither ion can penetrate the intestine in appreciable amounts, are very effective, although not necessarily more so, than compounds in which only one ion is not absorbed.

The frequent use of salines is inadvisable because it increases the possibility of dehydration.

In addition to the use of this compound in saline laxatives, it is used in the packaged cheese industry as an emulsifying agent. Because packaged cheese is made from natural cheeses of varying characteristics it is found that they sometimes tend to "oil off," *i. e.*, form globules of fat on their surface. The addition of a small amount of disodium phosphate or tetrasodium pyrophosphate (a derivative) prevents this "oiling off."

<sup>1</sup> Green, M. W., J. Am. Pharm. Assn. (Pr. Ed.), 7, 347 (1946).

It is also used in the adjustment of calcium-phosphorus ratios in prepared milk and ice cream. Its action is that of an emulsifier, tending to prevent agglomeration of solids, and insures a smooth, creamy consistency. Average dose—4 Gm. (approximately 1 drachm).

2. *Effervescent Sodium Phosphate* (*Sodii Phosphas Effervescens*), U. S. P. XIII.—This preparation contains 20 per cent of Exsiccated Sodium Phosphate (see preparation 3) together with sodium bicarbonate and tartaric and citric acids. This preparation is used as a palatable laxative, the palatability being improved by the carbonation from the interaction of sodium bicarbonate and the organic acids. Average dose—10 Gm. (approximately 2½ drachms).

3. *Exsiccated Sodium Phosphate* (*Sodii Phosphas Exsiccatus*, Dried Sodium Phosphate), U. S. P. XIII.—“Exsiccated Sodium Phosphate, when dried at 110° to constant weight, contains not less than 98 per cent of  $\text{Na}_2\text{HPO}_4$ .” It is prepared by allowing the crystals of sodium phosphate to effloresce for several days in warm air at a temperature of from 25° to 30° C. The drying is continued in an oven, the temperature of which is gradually raised to 110° C. When the salt ceases to lose weight, it is powdered, sifted, and stored in well-closed containers. Too high a temperature at the beginning of the exsiccation causes the salt to dissolve in its own water of hydration and it is then difficult to expel traces of water from the hard, caked residue left upon evaporation of this solution. It is used principally in the preparation of Effervescent Sodium Phosphate. Average dose—2 Gm. (approximately 30 grains).

4. *Methylrosaniline Chloride Jelly* (*Gelatum Methylrosanilinae Chloridi*, Gentian Violet Jelly), N. F. VIII.—This preparation contains 0.43 per cent of exsiccated sodium phosphate. The sodium phosphate acts as a buffer to prevent development of acidity in the preparation which would lessen the efficacy of the drug. This preparation is used as an efficient application to burned areas. The use of a jelly is said to give results far superior to those experienced with application of aqueous solutions alone.

5. *Pepsin Elixir* (*Elixir Pepsini*), N. F. VIII.—This preparation contains in addition to other ingredients (pepsin, citric acid, distilled water, glycerin and aromatic elixir) 1.3 per cent of exsiccated sodium phosphate. The sodium phosphate together with the citric acid establishes a pH of approximately 4.5, at which point the proteolytic property of the pepsin is the most stable. The N. F. notes that to insure the dispensing of this elixir at standard strength it is required that an excess of pepsin be used in preparing it. Average dose—8 cc. (approximately 2 fluidrachms).

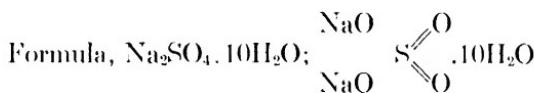
6. *Sodium Phosphate Solution* (*Liquor Sodii Phosphatis*), N. F. VIII.—“Sodium Phosphate Solution contains, in each 100 cc., not less than 37 Gm. and not more than 41 Gm. of  $\text{Na}_2\text{HPO}_4$ .” It is prepared by dissolving 400 Gm. of Exsiccated Sodium Phosphate (or an equivalent quantity of the crystallized form) together with 130 Gm. of citric acid and 150 cc. of glycerin in enough distilled

water to make 1000 cc. of finished preparation. If the crystallized form is used, the water present as water of crystallization should be deducted from the amount of water called for by the formula. The presence of a small amount of sodium hydrogen citrate (formed when sodium phosphate and citric acid react) and of glycerin tend to prevent crystallization. It is used for its laxative properties. Average dose—8 cc. (approximately 2 fluidrachms).

7. *Sodium Thiocyanate Elixir* (Elixir Sodii Thiocyanatis, Elixir of Sodium Sulfocyanate), N. F. VIII.—This preparation contains 40 Gm. each of sodium thiocyanate and sodium phosphate (not exsiccated) in every 1000 cc. The preparation is used in the treatment of essential hypertension (see p. 215). Average dose—4 cc. (approximately 1 fluidrachm).

## SODIUM SULFATE

### *Sodium Sulfate*, U. S. P. XIII



Molecular Weight, 322.21

**Physical Properties.**—Sodium Sulfate occurs in large, colorless, transparent, monoclinic crystals or smaller granular crystals, which are odorless and have a saline, bitter taste. Because the vapor pressure of the decahydrate is larger than the mean vapor tension of the moisture in the air, the crystals effloresce rapidly on exposure to air and become covered with a white powder of anhydrous sodium sulfate. The crystals have a specific gravity of 1.492 at 20° C.

One Gm. of Sodium Sulfate dissolves in about 8 cc. of water at 0° C., in 1.5 cc. of water at 25° C., in 0.28 cc. of water at 34° C. (temperature of greatest solubility) and in 0.42 cc. of water at 100° C. It is insoluble in alcohol but dissolves in glycerin.

At about 33° C. Glauber's salt melts in its water of hydration to form a supersaturated solution, and part of the anhydrous salt separates out. When the heating is continued at 100° C., all of the water (about 56 per cent) is driven off, and there remains an anhydrous sodium sulfate which fuses without decomposition at about 886° C.

**Chemical Properties.**—The principal chemical properties of sodium sulfate deal with the precipitation of the sulfate ion in the form of insoluble salts. Almost all sulfates are freely soluble, but there are several notable exceptions, namely  $\text{BaSO}_4$ ,  $\text{CaSO}_4$ ,  $\text{SrSO}_4$  and  $\text{PbSO}_4$ . Addition of soluble salts of the above cations to solutions of  $\text{Na}_2\text{SO}_4$  will cause precipitation of the corresponding sulfates.

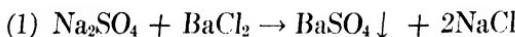
The anhydrous salt readily hydrates itself to form the decahy-

drate, and for this reason is used as a drying agent for organic liquids such as ether, chloroform, etc.

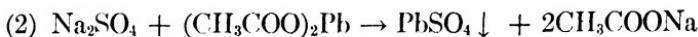
**Official Tests for Identity.**—1. Solutions of sodium sulfate (1 in 20) respond to all tests for *Sodium* (*q. v.*).

2. Solutions of the salt also respond to all tests for *Sulfate*:

(a) Upon addition of barium chloride T.S., a precipitate of  $\text{BaSO}_4$  is formed (1). The precipitate is insoluble in hydrochloric or nitric acids.



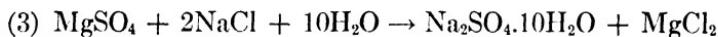
(b) Lead acetate T.S. will produce a white precipitate of lead sulfate (2) which is soluble in ammonium acetate solution.



(c) No precipitate results upon the addition of hydrochloric acid which differentiates the salt from sodium thiosulfate which does form a precipitate (see p. 216).

**Commercial Manufacture.**—Sodium sulfate is found either with or without water of hydration in large saline deposits in Spain, Siberia, Sicily, Italy, Germany, North Dakota and Canada. It also occurs in many mineral waters (*q. v.*). The crystallized anhydrous salt is found in the form of *thenardite*, and the hydrous salt ( $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ ) occurs as *mirabilite* or Glauber's salt. It is found at Stassfurt in monoclinic crystals as *glauberite* ( $\text{Na}_2\text{SO}_4 \cdot \text{CaSO}_4$ ).

Sodium sulfate is obtained by evaporating and cooling the mother liquors (which contain magnesium sulfate and sodium chloride) obtained in the recovery of sodium chloride from sea water (3). (See p. 175.)



The mother liquors obtained by the treatment of carnallite or kieserite contain about 25 per cent of magnesium sulfate and 50 per cent of sodium chloride. At Stassfurt, these liquors are evaporated at a temperature of about  $33^\circ \text{C}$ . to a gravity of approximately  $34^\circ \text{ Baumé}$ , and the sodium sulfate allowed to crystallize in large tanks during the cold winter nights. In this manner, large crystals containing 12 molecules of water of hydration are obtained.

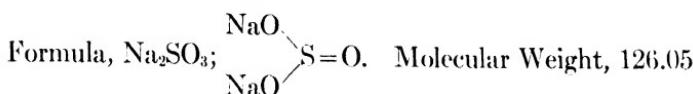
Much of the sodium sulfate of commerce is obtained from the manufacture of hydrochloric acid (*q. v.*) and nitric acid (*q. v.*). Indeed, these methods of manufacturing the acids have probably survived because of the need for sodium sulfate in various industries.

**Pharmaceutical Preparations and Uses.**—1. *Sodium Sulfate* (*Sodii Sulfas*, Glauber's Salt), U. S. P. XIII.—“Sodium Sulfate, when dried to constant weight at  $110^\circ$ , contains not less than 99 per cent of  $\text{Na}_2\text{SO}_4$ .” Sodium sulfate is used therapeutically as a saline laxative (see p. 209). Although its taste and drastic action is a distinct disadvantage it is considered to be one of the most effective of the saline cathartics. Large quantities are used in

veterinary practice as a cathartic. Average dose—15 Gm. (approximately 4 drachms).

### SODIUM SULFITE, EXSICCATED

*Exsiccated Sodium Sulfite, U. S. P. XIII*

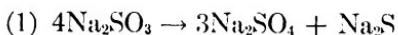


**Physical Properties.**—Exsiccated Sodium Sulfite occurs as a white, odorless powder. It has a cooling, saline, sulfurous taste. It undergoes oxidation in air.

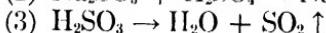
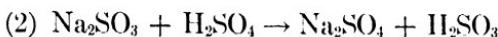
One Gm. is soluble in about 4 cc. of water at 25° C. It is sparingly soluble in alcohol.

**Chemical Properties.**—Aqueous solutions of the salt are alkaline to litmus paper and to phenolphthalein because of hydrolysis.

Heating of the dry salt in a closed tube causes the formation of both sodium sulfide and sodium sulfate (an internal oxidation-reduction) (1).

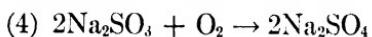


Aqueous solutions of sodium sulfite when acidulated with sulfuric acid (or hydrochloric acid) readily liberate sulfur dioxide (2, 3).



Sodium sulfite solutions will produce a precipitate of the corresponding sulfite with solutions of the soluble salts of calcium, strontium, barium, lead and silver.

One of the principal chemical properties of the sulfites is their marked reducing action. This is exhibited in a number of ways. For example, sodium sulfite is added to boiler feed water to take up the dissolved oxygen (4) which causes corrosion.



Iodine is readily reduced to the colorless iodide form by acidified solutions of sodium sulfite (5).



Hydrogen sulfide is readily acted upon by acidified solutions of sodium sulfite (6) (oxidizing action).

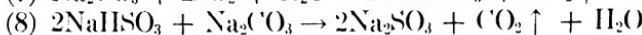


**Official Tests for Identity.**—1. A solution (1 in 20) of the salt responds to the tests for *Sodium* (*q. v.*).

2. A solution also responds to all tests for *Sulfite*: Sulfites, when treated with hydrochloric acid, liberate colorless fumes (2, 3) of

sulfur dioxide having an odor of burning sulfur. This gas blackens filter paper moistened with mercurous nitrate T.S.

**Commercial Manufacture.**—Normal sodium sulfite is prepared by saturating a solution of sodium carbonate with SO<sub>2</sub> (7) and then adding a quantity of sodium carbonate, previously dissolved in water, equal to that originally used (8). The solution is evaporated to crystallization, and the dried crystals exsiccated in the usual way.



**Pharmaceutical Preparations and Uses.**—1. *Exsiccated Sodium Sulfite* (Sodii Sulfis Exsiccatus), U. S. P. XIII.—“Exsiccated Sodium Sulfite contains not less than 95 per cent of Na<sub>2</sub>SO<sub>3</sub>.” A 10 per cent solution is sometimes used as a treatment for ringworm and other parasitic skin diseases. Industrially it is used as an antioxidant and as an antichlor.

2. *Tannic Acid Glycerite* (Glyceritum Acidi Tannici, Glycerite of Tannin), U. S. P. XIII.—In addition to other ingredients (tannic acid, sodium citrate and glycerin) this preparation contains 0.1 per cent of exsiccated sodium sulfite to prevent oxidative changes in the tannic acid. This preparation is used in burn therapy.

3. *Tannic Acid Ointment* (Unguentum Acidi Tannici), U. S. P. XIII.—In addition to other ingredients (tannic acid, glycerin and yellow ointment) this preparation contains 0.2 per cent of exsiccated sodium sulfite. Its use in this preparation is the same as in the glycerite above, namely to prevent oxidation of the tannic acid with resultant discoloration of the ointment. A caution is given by the N. F., *viz.*, to avoid the use of iron utensils or containers in the preparation and storage of the ointment because of the possibility of forming dark-colored iron tannate. This ointment is also intended for burn therapy.

## SODIUM THIOCYANATE

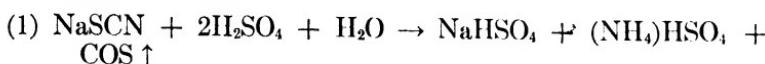
### *Sodium Thiocyanate*, N. F. VIII

Formula, NaSCN. Molecular Weight, 81.08

**Physical Properties.**—Sodium Thiocyanate (medicinal) is obtained as small, colorless, hygroscopic crystals, or as a white powder which is affected by light. It has a cooling, saline taste.

One Gm. of Sodium Thiocyanate is soluble in about 0.7 cc. of water or in about 4 cc. of alcohol at 25° C.

**Chemical Properties.**—Thiocyanates in general are decomposed by the addition of approximately 35 per cent sulfuric acid to aqueous solutions (1) although the addition of more dilute (5 per cent) sulfuric acid is without effect.



The addition of certain metallic cations, namely  $\text{Ag}^+$ ,  $\text{Hg}^{++}$ ,  $\text{Cu}^{++}$ ,  $\text{Au}^{+++}$  and  $\text{Pb}^{++}$ , to solutions of thiocyanates causes the precipitation of the corresponding insoluble thiocyanate.

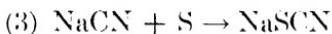
Addition of ferric salts to solutions of thiocyanates causes the formation of a blood-red color which has been variously ascribed to the formation of  $\text{Fe}(\text{CNS})_3$ ,  $\text{Fe}(\text{CNS})_2^-$  and  $\text{Fe}(\text{CNS})^{++}$ . The latter postulation,<sup>1</sup> based on dilution experiments and experiments on the migration of ions in an electric field, seems to explain the facts most satisfactorily (2). The addition of hydrochloric acid to the solution does not affect the color but, in fact, favors it by suppressing hydrolysis of the  $\text{Fe}^{+++}$  which indirectly increases the ferriion concentration.



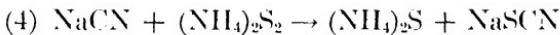
**Official Tests for Identity.**—1. Aqueous solutions of sodium thiocyanate (1 in 20) respond to all tests for *Sodium* (*q. v.*).

2. Aqueous solutions also respond to the test for *Thiocyanate* which consists of the addition of ferric chloride T.S. to obtain a red color (2) which is not destroyed by moderately concentrated mineral acids.

**Commercial Manufacture.**—Sodium thiocyanate is made from sodium cyanide and sulfur by simply heating the two together (3).



It may also be made by adding ammonium polysulfide to sodium cyanide (4).



**Pharmaceutical Preparations and Uses.**—1. *Sodium Thiocyanate* (Sodii Thiocyanas, Sodium Sulfocyanate), N. F. VIII.—“Sodium Thiocyanate, when dried to constant weight at 110°, contains not less than 98.5 per cent of NaSCN.” This drug has been used in the treatment of arterial hypertension. The opinions as to the efficacy and dangers involved in its use are varied. In general, it is quite useful in the management of hypertension, but its use should be safeguarded by a close control of the thiocyanate level in the blood (8 to 12 mg. per 100 cc. is considered safe and effective). Elderly people (over 60) do not tolerate the drug very well. Weakness and fatigue are commonly experienced in the early stages of thiocyanate therapy, occurring in many cases prior to any relief of the hypertension. Average dose—0.3 Gm. (approximately 5 grains).

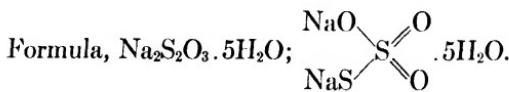
2. *Sodium Thiocyanate Elixir* (Elixir Soda Thiocyanatis, Elixir of Sodium Sulfocyanate), N. F. VIII.—This elixir contains 4 per cent of sodium thiocyanate together with numerous other ingredients. It is simply a liquid preparation for the administration of

<sup>1</sup> Bent and French, J. A. C. S., 63, 568 (1941); also Edmonds and Birnbaum, *Ibid.*, 63, 1471 (1941).

the thiocyanate for the relief of hypertension. Average dose—4 cc. (approximately 1 fluidrachm).

### SODIUM THIOSULFATE

*Sodium Thiosulfate*, U. S. P. XIII



Molecular Weight, 248.19

**Physical Properties.**—Sodium Thiosulfate occurs in large, transparent, colorless, monoclinic prisms or as a coarse, crystalline powder. It is odorless and has a cooling, bitter taste. It has a specific gravity of 1.729 at 17° C. The salt is stable in air below 33° C., but effloresces in dry air above that temperature. It deliquesces in moist air.

One Gm. of sodium thiosulfate dissolves in 0.5 cc. of water at 25° C. Aqueous solutions of the salt decompose upon boiling. It is insoluble in alcohol.

**Chemical Properties.**—At 56° C. the salt melts in its water of hydration and at 100° C. it becomes anhydrous. At 100° C. decomposition of the salt begins and at 220° C. it is completely converted into sulfur, sulfur dioxide, sodium sulfide and sodium sulfate (1, 2 and 3).

- (1)  $4\text{Na}_2\text{S}_2\text{O}_3 \rightarrow 3\text{Na}_2\text{SO}_4 + \text{Na}_2\text{S}_5$
- (2)  $\text{Na}_2\text{S}_5 \rightarrow \text{Na}_2\text{S} + 4\text{S} \uparrow$
- (3)  $\text{Na}_2\text{S}_5 + 4\text{O}_2 \rightarrow \text{Na}_2\text{S} + 4\text{SO}_2 \uparrow$

Aqueous solutions are neutral or slightly alkaline (hydrolysis).

The addition of acids, *e. g.*, hydrochloric acid, to a solution of sodium thiosulfate liberates thiosulfuric acid (4) which instantly decomposes into sulfur, sulfur dioxide, and water (5).

- (4)  $\text{Na}_2\text{S}_2\text{O}_3 + 2\text{HCl} \rightleftharpoons \text{H}_2\text{S}_2\text{O}_3 + 2\text{NaCl}$
- (5)  $\text{H}_2\text{S}_2\text{O}_3 \rightleftharpoons \text{S} \downarrow + \text{H}_2\text{SO}_3 \rightleftharpoons \text{H}_2\text{O} + \text{SO}_2 \uparrow$

Although the alkali thiosulfates are very soluble in water, most of the other thiosulfates are difficultly soluble and therefore addition of metallic cations other than the alkali cations may reasonably be expected to cause precipitation of the corresponding insoluble thiosulfate.

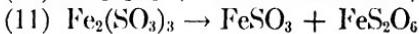
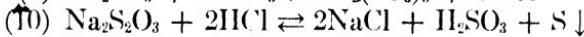
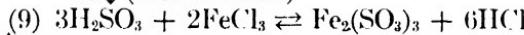
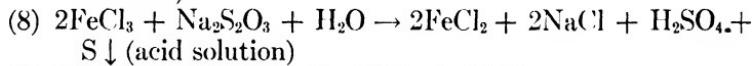
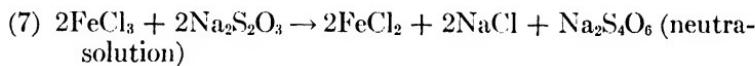
The principal chemical property exhibited by thiosulfates in general is that of reduction. The pronounced reducing power of sodium thiosulfate, for example, is shown by the effect on iodine (6).

- (6)  $2\text{Na}_2\text{S}_2\text{O}_3 + \text{I}_2$  (colored)  $\rightarrow 2\text{NaI}$  (colorless) +  $\text{Na}_2\text{S}_4\text{O}_6$  (colorless)

Solutions of iodine are colored, but the addition of sodium thiosulfate causes immediate decolorization by the formation of colorless

sodium iodide and sodium tetrathionate. The reaction is so clean-cut that use is made of it in quantitative analysis for determining amounts of iodine in unknown samples.

The reducing action is also shown by the reduction of ferric salts to the corresponding ferrous form (7, 8). Upon the addition of a drop or two of ferric chloride T.S. to a solution of sodium thiosulfate, a dark violet color is formed and then quickly disappears. The fugitive violet color has not been adequately explained, some suggesting that it may be due to formation of ferric thiosulfate and still others that it is due to the formation of ferric sulfite,  $\text{Fe}_2(\text{SO}_3)_3$ . The ferric sulfite is said to be formed by a reaction between ferric chloride and sulfurous acid (9), the latter having been developed by the action of some free hydrochloric acid in the ferric chloride test solution upon the sodium thiosulfate (10). The ferric sulfite (red color) would soon be reduced to ferrous sulfite with the subsequent disappearance of the color (11).



**Official Tests for Identity.**—1. Solutions of Sodium Thiosulfate (1 in 20) respond to all tests for *Sodium* (*q. v.*).

2. Solutions of the salt also respond to all tests for *Thiosulfate*:

(a) Upon the addition of hydrochloric acid, a white precipitate of sulfur is formed. This changes to the yellow form of sulfur and sulfur dioxide (4, 5) is liberated.

(b) Addition of ferric chloride T.S. causes the formation of a dark violet color which quickly disappears (9, 10, 11).

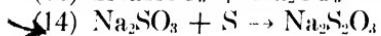
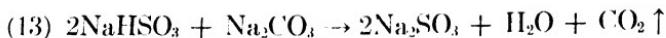
(c) Iodine solutions are quickly decolorized by means of sodium thiosulfate (6).

**Commercial Manufacture.**—1. Soda ash (crude sodium carbonate) is dissolved in hot water and the solution (26° Baumé) is allowed to flow down over hardwood sticks contained in an absorption tower, where it meets an ascending current of gas weak in sulfur dioxide. The soda ash absorbs all of the sulfur dioxide and then flows down a second tower in which it contacts gases coming directly from the sulfur burner and hence rich in sulfur dioxide (12).

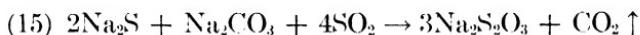


The bisulfite liquor is then treated with soda ash to change it into neutral sodium sulfite (13) and this is heated with powdered brimstone in a brick-lined cast iron vessel that is provided with a stirrer (14). The resulting solution of sodium thiosulfate is concentrated, allowed to settle, and run into lead-lined crystallizers to cool and

crystallize. After several days the crystals are transferred to centrifugals, washed free from mother liquor by a short spraying with water, and screened to size.



2. The more important of the two commercial processes makes use of by-product sulfide liquors, which contain about 8 per cent of sodium sulfide ( $\text{Na}_2\text{S}$ ) and 6 per cent of sodium carbonate ( $\text{Na}_2\text{CO}_3$ ). When these liquors are rapidly circulated through a tower filled with wooden shelves, they meet an ascending current of sulfur dioxide, obtained from any one of the usual sources (15). After the liquors have absorbed a sufficient amount of the gas, they are filter-pressed, and concentrated in a steel boiler. The crystallization, etc., is carried out as described in the process immediately preceding.



**Pharmaceutical Preparations and Uses.**—1. *Sodium Thiosulfate* (Sodii Thiosulfas, "Sodium Hyposulfite"), U. S. P. XIII.—"Sodium Thiosulfate, when dried at  $100^\circ$  to constant weight, contains not less than 99 per cent of  $\text{Na}_2\text{S}_2\text{O}_3$ ." The common name of this compound, "sodium hyposulfite," is a misnomer. Sodium hyposulfite is really  $\text{Na}_2\text{S}_2\text{O}_4$  (also sodium hydrosulfite). However, through common usage, the term is still used for sodium thiosulfate and is sometimes shortened to "hypo." Sodium thiosulfate is infrequently used as a cathartic and as an antiseptic in fermentative dyspepsia. It is often used as an external application or wash to combat ringworm and other parasitic skin diseases. Its action in these cases is probably due to the formation of decomposition products (*e. g.*, sulfur, etc.) rather than to any antiseptic action inherent in the compound. Its external use as a wash in poison ivy cases is unfounded and probably of little value. The salt has been used intravenously in the treatment of dermatitis caused by reactions from the arsphenamines and mercurials as well as in the treatment of poisoning from other heavy metals. Its value in this connection is probably due to formation of sulphydryl ( $-SH$ ) groups which detoxify the poison. This theory is supported by the striking effect of BAL (British Anti-Lewisite), which contains sulphydryl groups, in the treatment of arsenic poisoning.

The use of sodium thiosulfate in cyanide poisoning has been considered (see p. 204). Average dose—oral or intravenous, 1 Gm. (approximately 15 grains).

2. *Sodium Thiosulfate Ampuls* (Ampullæ Sodii Thiosulfatis, Sodium Hyposulfite Injection), N. F. VIII.—These ampuls "contain a sterile solution of sodium thiosulfate in freshly boiled water for injection, and yield  $\text{Na}_2\text{S}_2\text{O}_3$ , equal to not less than 61 per cent and not more than 67 per cent of the labeled amount of  $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$ ."

These ampuls are used for the intravenous injection of sodium thiosulfate in the treatment of arsenical (arsphenamine) as well as in lead, bismuth and mercury poisoning. It is marketed in 5 or 10 per cent concentrations in 10-cc. ampuls. From 0.5 to 1 Gm. is given daily until symptoms are relieved, although as much as 6 Gm. of the salt on three successive days has been advocated in mercury poisoning. Average dose—1 Gm. of Sodium Thiosulfate.

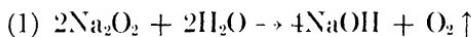
3. *Potassium Iodide Solution* (Liquor Potassii Iodidi, Saturated Potassium Iodide Solution), N. F. VIII.—“Potassium iodide solution contains, in each 100 cc., not less than 97 Gm. and not more than 103 Gm. of KI.” The N. F. notes that if the solution is not to be used immediately it is desirable to add 0.5 Gm. of sodium thiosulfate per liter of finished solution. The function of the sodium thiosulfate in this case would, of course, be to reduce any free iodine that might form in the solution to the iodide.

This solution is used in iodide therapy (see p. 95). Average dose—0.3 cc. (approximately 5 minimis).

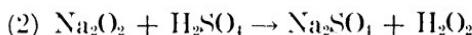
#### NON-OFFICIAL COMPOUNDS OF SODIUM

**Sodium Peroxide** (Sodii Peroxidum), N. N. R. (1947),  $\text{Na}_2\text{O}_2$ , Molecular Weight, 78.00.

This compound occurs as a white or yellowish, amorphous powder. It reacts readily with water to form sodium hydroxide and oxygen (1).



As previously shown (see p. 58), it will react with cold acids to form a solution of hydrogen peroxide (2).



The compound is a very powerful oxidizing agent as evidenced by its easy liberation of oxygen on contact with water.

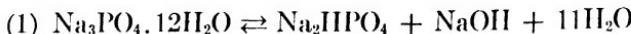
By placing anhydrous sodium peroxide on a watch glass in a confined area with a dish of water near it, it is possible to convert the sodium peroxide to an octahydrate ( $\text{Na}_2\text{O}_2 \cdot 8\text{H}_2\text{O}$ ) which may be dissolved in water without the evolution of oxygen. This octahydrate, when dehydrated over concentrated sulfuric acid in a desiccator changes to a dihydrate ( $\text{Na}_2\text{O}_2 \cdot 2\text{H}_2\text{O}$ ).

The salt is prepared commercially by burning dry sodium in air.

Sodium peroxide is never used internally but has been employed in the form of a paste in the treatment of acne and, when incorporated in a soap, to remove blackheads (comedones).

**Sodium Phosphate, Tribasic** (Trisodium Phosphate, Normal Sodium Phosphate),  $\text{Na}_3\text{PO}_4 \cdot 12\text{H}_2\text{O}$ , Molecular Weight, 380.16.—This compound occurs as colorless or white crystals which are soluble in about 5 parts of water but insoluble in alcohol. It is stable only in the solid state.

When dissolved in water it is converted immediately into disodium hydrogen phosphate and sodium hydroxide, both of which contribute to the alkalinity of the solution (1). Its alkalinity contributes to its use as a water softener and general cleansing agent.



When rapidly heated, the salt melts at about 75° C., but does not lose its last molecule of water of crystallization even on moderate ignition.

Most of the trisodium phosphate (commonly known as TSP) is made from phosphoric acid which is first neutralized with soda ash ( $\text{Na}_2\text{CO}_3$ ) to obtain disodium phosphate (2) and then treated with sufficient caustic soda ( $\text{NaOH}$ ) to complete the reaction (3).



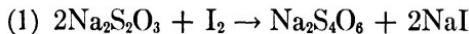
The solution is concentrated to obtain crystals. The crystallization of trisodium phosphate is one of the most carefully conducted operations in its entire manufacture. Small crystals, although prone to cake in moist weather, are more desirable than the larger coarse crystals because they dissolve much faster in water, a property which is of importance in packaged cleaners and water softeners.

Technical grades are employed in laundering, in photographic developers, for softening water and in the paper, sugar and tanning industries. It is rarely, if ever, used for medicinal purposes.

**Sodium Tetrathionate**,  $\text{Na}_2\text{S}_4\text{O}_6 \cdot \text{H}_2\text{O}$ , Molecular Weight, 288.23. -- This compound occurs as colorless or white crystals which are freely soluble in water. It contains 44 per cent of sulfur as contrasted to sodium thiosulfate (for which it is recommended as a substitute) which contains only 26 per cent.

Although this compound is said to be more or less stable it has been found by experience that toxic effects occur from improperly stabilized preparations. The means of stabilization is a trade secret and is not published.

The compound is manufactured from sodium thiosulfate by the classical method of oxidizing the thiosulfate with an excess of iodine (1), following which, it is precipitated as a dihydrate, washed and dried.



The purification of the crude sodium tetrathionate is said to be one of the most difficult steps in the entire manufacturing process. A process has been evolved whereby the precipitated dihydrate is converted to a monohydrate. During the loss of the one molecule of water the physical properties of the salt change from that of a dense compact crystal to a loose fluffy mass. The enormously increased surface area and decreased particle size permit much more thorough washing, and as a consequence a product that is free from traces of iodine or sodium iodide.

This preparation is marketed under the trade name of "Tetra-thione" and is indicated in the treatment of peripheral circulatory diseases (such as Buerger's disease and Raynaud's disease), essential hypertension, thrombi and emboli, and in metallic poisoning.<sup>1</sup> Its action in the body is to increase the oxygen capacity of the blood, decrease its viscosity, and also to prolong the coagulation time. From these considerations it is apparent that the blood circulation to the affected periphery (hands and feet) will be improved by its administration. It is administered intravenously and is used in doses of 0.6 Gm. per day if necessary.

<sup>1</sup> See, however, J. A. Ph. A., **8**, 266, 1947, and ibid., **8**, 574, 1947, for A. M. A. Council Reports on this compound.

## CHAPTER XII

### POTASSIUM AND POTASSIUM COMPOUNDS

#### POTASSIUM

Symbol, K. Valence, 1. Atomic Weight, 39.096; Atomic Number, 19.

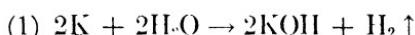
**History.**—Some compounds of potassium have been known since the earliest times. In 1807, Sir Humphrey Davy isolated the element from potash (a residue left after the evaporation of a solution obtained by leaching ashes and which was considered to be elemental in character) by placing a piece of it on a platinum plate which formed the negative pole of a series of electric batteries, and touching the substance with a platinum wire connected to the positive pole. An energetic action took place and minute, metallic globules of potassium were formed on the plate. Some of these globules burst into flame and others merely tarnished. In 1808 Gay-Lussac and Thénard obtained the metal by passing molten potash through a clay tube containing iron turnings heated to white heat. The researches by Gay-Lussac and Thénard (1811) established potassium as a metallic element.

**Occurrence.**—Potassium is never found free in Nature, but in combination the metal is widely and abundantly distributed. Potassium compounds are present in sea water and comprise 2.6 per cent of the earth's crust. Potassiferous silicates, *e. g.*, *orthoclase* (feldspar) ( $KAlSi_3O_8$ ), potash mica, etc., occur universally but are not used commercially as sources of potassium. Silicates containing potassium are omnipresent in almost all rocks and their disintegration provides the soluble potassium salts found in all fertile soils. These salts are assimilated by plants and converted into the potassium salts of such organic acids as oxalic, tartaric, succinic, etc., which, when the plants are burned, are converted into potassium carbonate. Potash forms over 90 per cent of the total alkali in the ashes of most plants. Enormous deposits of various potassium-containing minerals are located at Stassfurt, Germany, and near Carlsbad, N. M. These deposits, in addition to sodium chloride, contain *sylvite* ( $KCl$ ); *carnallite* ( $KCl \cdot MgCl_2 \cdot 6H_2O$ ); *kainite* ( $K_2SO_4 \cdot MgSO_4 \cdot MgCl_2 \cdot 6H_2O$ ); *polyhalite* ( $MgSO_4 \cdot K_2SO_4 \cdot 2CaSO_4 \cdot 2H_2O$ ); and other minerals of minor value. These minerals are of industrial importance because of their solubility in water and the ease with which they can be worked chemically.

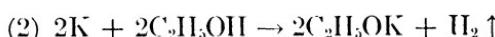
At present the potassium needs of the United States are obtained from Searles Lake at Trona, California, where it occurs as  $KCl$  and  $K_2SO_4$ , and from mines in New Mexico and Texas, where it occurs as polyhalite.

**Physical Properties.**—When newly cut, potassium is a silver-white metal. The color changes rapidly to a grayish-white having a bluish tinge. It is slightly softer than sodium and has lower boiling-and melting-points. The metal dissolves in liquid ammonia, forming a blue solution. Upon exposure to the atmosphere potassium immediately forms a film of oxide. At ordinary temperatures the metal is of waxy consistency and may be kneaded with the fingers and cut with a dull knife. At temperatures below 0° C. it is quite hard and brittle. It has a specific gravity of 0.86 (20° C.), a melting-point of 62.3° C. and boils at 760° C. emitting a green vapor containing monatomic molecules. Potassium has been crystallized in bluish-green quadratic octahedra.

**Chemical Properties of Potassium and Potassium Ion.**— When potassium is heated in air it fuses and then inflames, producing a mixture of oxides ( $K_2O$ ,  $K_2O_2$ , etc.). In behavior it resembles sodium very closely but it is a little more reactive. The element combines violently with sulfur, oxygen and the halogens. Potassium decomposes water with the evolution of hydrogen and the formation of the hydroxide (1).



The hydrogen immediately ignites and at the high temperature a part of the potassium is vaporized giving a violet color to the flame. Because of the ease with which potassium is oxidized and also because of its great affinity for water, the metal is kept under kerosene, petroleum, benzene, benzine, or other liquids that are free from oxygen and are immiscible with water. Potassium also reacts with ethyl alcohol to form potassium ethylate and hydrogen (2). In this case the hydrogen does not inflame.



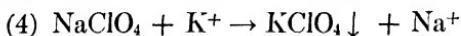
When hydrogen is passed over metallic potassium heated to 360° C., a white crystalline hydride ( $KH$ ) is formed.

Potassium amide ( $KNH_2$ ) is formed by passing ammonia over heated potassium whereby one-third of the hydrogen is replaced by potassium. Potassium has been shown to be slightly radioactive. It also has interesting photoelectric sensitivity because it emits electrons when exposed to light.

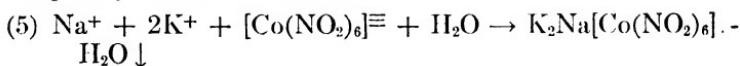
Potassium ion will form a precipitate by adding a drop of a solution of chloroplatinic acid ( $H_2PtCl_6$ ) to 1 cc. of a neutral or acid solution (with hydrochloric acid) of the salt (3). The yellow crystalline precipitate of potassium chloroplatinate ( $K_2PtCl_6$ ) so formed is almost insoluble in 80 per cent alcohol. This reaction is useful in determining potassium quantitatively. Small amounts of potassium may be detected by making the above test in the presence of alcohol on a slide and observing the crystals with a microscope.



Sodium perchlorate ( $\text{NaClO}_4$ ) precipitates from solutions of potassium salts, potassium perchlorate ( $\text{KClO}_4$ ) (4) which is only slightly soluble in water and nearly insoluble in 95 per cent alcohol.

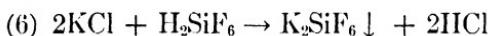


If a neutral solution of a potassium salt is made slightly acid with acetic acid and then added to a solution of sodium cobaltic nitrite,  $\text{Na}_3\text{Co}(\text{NO}_2)_6$ , a double salt of potassium sodium cobaltic nitrite,  $\text{K}_2\text{Na}[\text{Co}(\text{NO}_2)_6]\cdot\text{H}_2\text{O}$ , is precipitated (5). In concentrated solutions the precipitate is formed immediately but in weak solutions the mixture must be allowed to stand for some time. Potassium cobaltic nitrite is sparingly soluble in water (1 to 11,000 at 15° C.) and completely insoluble in alcohol.

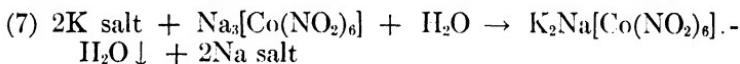


Picric acid,  $\text{C}_6\text{H}_2(\text{NO}_2)_3\text{OH}$ , or sodium picrate, precipitate yellow crystalline potassium picrate,  $\text{C}_6\text{H}_2(\text{NO}_2)_3\text{OK}$ , from a solution of a potassium salt.

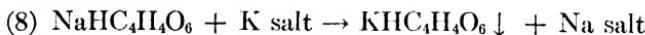
If a solution of a soluble potassium salt is treated with a solution of hydrofluosilicic acid, sparingly soluble potassium silicofluoride is formed (6)



Sodium cobaltic nitrite test solution produces a yellow precipitate with saturated aqueous solutions of a potassium salt (7).



Sodium bitartrate precipitates granular crystalline potassium hydrogen tartrate ( $\text{KHC}_4\text{H}_4\text{O}_6$ ) from concentrated solutions of potassium salts (8). The precipitate is soluble in ammonia T.S., in alkali hydroxides or carbonates and is insoluble in alcohol. Agitation, alcohol, or a little glacial acetic acid increases the speed of the precipitation.

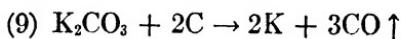


Potassium and most potassium salts impart a violet color to a non-luminous flame. If sodium is also present, the yellow sodium flame obscures the violet color unless a blue glass or preferably a saturated solution of potassium chrome alum is interposed between the flame and the eye.

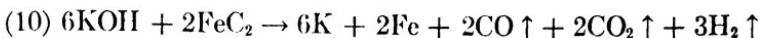
**Official Tests for Identity.**—1. Potassium compounds impart a violet color to a non-luminous flame (*q. v.*).

2. Sodium bitartrate T.S. produces a white, crystalline precipitate (8) (*q. v.*).

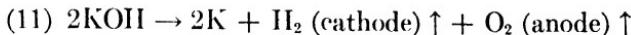
**Commercial Manufacture.**—Potassium metal has been prepared commercially by several methods. The (1) Brunner's process, which consists in the reduction of potassium carbonate with charcoal (9),



(2) by the reduction of caustic potash with iron carbide (10).



(3) Castner's process, which consists of electrolyzing potassium hydroxide (11).



At present, nearly all of the metal is obtained by the electrolysis of potassium chloride. Potassium chloride fuses at 772° C. and since potassium boils at 760° C., considerable trouble was first encountered. A mixture of potassium chloride, potassium fluoride and barium chloride was found suitable. The Downs cell is used for the electrolysis. (See Sodium, p. 147.)

**Pharmacological Action of Potassium Ion.**—The potassium ion is the predominating ion within the cell and is necessary for cell growth and function. It is present in intracellular fluids in contrast to the sodium ion that is present in extracellular fluids. Potassium ion administered orally or by injection is rapidly absorbed. The kidney removes the excess potassium ions from the blood so quickly that at any one time there is slight change in blood concentration (0.3 Gm. per 1000 cc.). Since the tubules of the kidney do not allow the potassium ion to pass through their walls an osmotic pressure is established causing water to pass from the blood into the tubule. By such an action the potassium ion exerts a diuretic effect. The functions of the nerves, nerve endings, cardiac muscle, and skeletal muscle are depressed by potassium ion, whereas smooth muscle is stimulated by it. These effects can be secured only by intravenous or hypodermic injections or by the oral administration of toxic doses.<sup>1</sup> Because of the rapid excretion of potassium ion (*via* urine, etc.) the oral administration of average doses of potassium salts produces only osmotic effects, *e. g.*, diuresis. Therefore, the therapeutic action of potassium salts cannot be markedly differentiated from those produced by the corresponding sodium salts.

#### OFFICIAL COMPOUNDS OF POTASSIUM

##### POTASSIUM ACETATE

*Potassium Acetate*, U. S. P. XIII

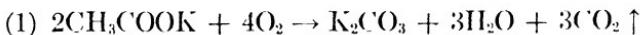
Formula,  $\text{CH}_3\text{COOK}$ . Molecular Weight, 98.14

**Physical Properties.**—Potassium Acetate occurs in the form of a white crystalline powder, or colorless, monoclinic crystals. When dry the salt is odorless but when slightly damp it has a faint acetous odor. It has a saline and slightly alkaline taste. It melts at 292° C., and has a density of 1.8. It absorbs moisture very rapidly when exposed to the air and hence must be kept in air-tight containers.

<sup>1</sup> It is only when very large doses of potassium salts are given, as, for example, after repeated 7-Gm. doses of potassium iodide in cases of late syphilis, that toxic effects from excess of potassium ions are noted.

One Gm. of Potassium Acetate is soluble in 0.5 cc. of water and in 3 cc. of alcohol, at 25° C. One Gm. is soluble in about 0.2 cc. of boiling water. It is insoluble in ether.

**Chemical Properties.**—Potassium acetate fuses when heated and upon strong ignition, decomposes into volatile, inflammable vapors and leaves a residue of potassium carbonate containing particles of carbon (1).



The residue gives positive tests for potassium ion (*q. v.*), is alkaline to litmus paper and effervesces with acids (carbonate).

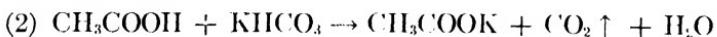
An aqueous solution of potassium acetate is alkaline to litmus. All of the acetates are soluble except the silver salt.

**Official Tests for Identity.**—1. Potassium acetate responds to all tests for the *Acetate* ion. (See Sodium Acetate, p. 149.)

2. Potassium acetate also responds to the test for the *Potassium* ion (*q. v.*).

**Commercial Manufacture.**—Potassium acetate is made by adding potassium carbonate or bicarbonate to acetic acid until effervescence ceases, evaporating the solution to dryness, fusing the residue, and allowing the mass to solidify. While still warm it is quickly powdered and bottled. When crystalline flakes are desired, the solution of potassium acetate is stirred continuously during the concentration and the resulting crystalline mass centrifuged in a current of dry warm air. For the neutralization of the acetic acid, potassium bicarbonate is preferred to the carbonate on account of its greater purity. If potassium carbonate is used, it is usually necessary to filter the solution of potassium acetate from insoluble matter before concentrating it.

**Laboratory Preparation.**—Add powdered potassium bicarbonate (about 6 Gm.) to 10 cc. of Acetic Acid until effervescence ceases (2). Filter the solution and evaporate on a water-bath, adding 1 or 2 drops of diluted acetic acid from time to time. When the solution becomes viscid, transfer the dish to a sand bath and continue the evaporation at a temperature not exceeding 140° C., stirring constantly. When dry, powder the residue in a current of warm dry air, and bottle immediately.



**Pharmaceutical Preparations and Uses.**—1. *Potassium Acetate* (*Potassii Acetas*), U. S. P. XIII.—Potassium Acetate, when dried to constant weight at 150°, contains not less than 99 per cent of  $\text{CH}_3\text{COOK}$ . The acetate of potassium is used mainly as a diuretic. It has no specific action. However, it does act by changing the physical properties of the body fluids and by functioning as an alkali after absorption. (See Sodium Acetate, p. 150.) Like the alkali salts of most organic acids, it is decomposed in the body with the formation of potassium bicarbonate (3).



This reaction takes place very quickly and completely. The action as an alkali is the same as that of carbonates and bicarbonates except that the gastric juice is not neutralized. Because of its deliquescent property, potassium acetate is never prescribed in the dry state but always in solution. Average dose—1 Gm. (approximately 15 grains).

2. *Buchu, Juniper and Potassium Acetate Elixir* (Elixir Buchu, Juniperi et Potassii Acetatis), N. F. VIII.—Fifty Gm. of potassium acetate are present in 1000 cc. of finished elixir. It contributes to the diuretic action of the preparation. Average dose—4 cc. (approximately 1 fluidrachm).

### POTASSIUM BICARBONATE

*Potassium Bicarbonate*, U. S. P. XIII

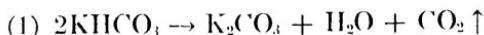


**History.**—Potassium bicarbonate was first prepared by mixing solutions of potassium carbonate and ammonium carbonate. Cartheuser discovered it in 1757. Cavendish is accredited with the process still used for its commercial manufacture.

**Physical Properties.**—Potassium Bicarbonate occurs in the form of white granules, a powder, or colorless, transparent, monoclinic prisms. It is odorless, and has a saline and slightly alkaline taste. It is stable in air. Any pronounced deliquescence is indicative of the presence of carbonate.

One Gm. of Potassium Bicarbonate is soluble in 2.8 cc. of water at 25° C. and in 2 cc. of water at 50° C. It is almost insoluble in alcohol. Its solutions are slightly alkaline to litmus paper, and neutral or very slightly alkaline to phenolphthalein T.S.

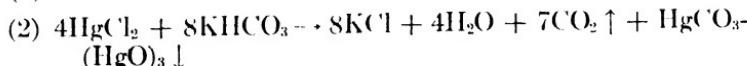
**Chemical Properties.**—When heated at 100° C. the salt slowly loses carbon dioxide and water and forms the normal carbonate (1).



This change is very rapid above 190° C.

When an aqueous solution of potassium bicarbonate is heated above 50° C., the salt loses carbon dioxide and water and, when the solution is boiled, it is completely converted to carbonate.

The addition of mercuric chloride test solution to an aqueous solution of potassium bicarbonate produces a faint murkiness which, as carbon dioxide is evolved, changes to a reddish-brown precipitate (2).



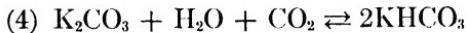
However, if the bicarbonate contains appreciable carbonate, a reddish-brown precipitate of a basic salt is produced immediately (3).



**Official Tests for Identity.**—1. Potassium bicarbonate gives all the tests for the *Bicarbonate* ion ( $\text{HCO}_3^-$ ). (See Sodium Bicarbonate, p. 153.)

2. An aqueous solution of the salt responds to all tests for *potassium* ion (*q. v.*).

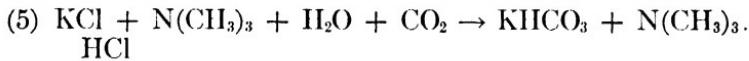
**Commercial Manufacture.**—1. Potassium bicarbonate is made by passing carbon dioxide through a very cold, saturated aqueous solution of the normal carbonate until the gas is no longer absorbed (4).



During the operation any silicates present in the carbonate solution are converted to bicarbonates and silica. The latter is filtered off. Then the filtrate is concentrated at a temperature not exceeding  $60^\circ\text{ C}$ . and upon cooling, anhydrous crystals of the salt are deposited.

2. A method also used is to pass carbon dioxide over a mixture of potassium carbonate and powdered charcoal which has been moistened with water. The mass is then lixiviated with water, filtered and concentrated. Large, monoclinic crystals of potassium bicarbonate separate out. They are permanent in air.

3. Potassium bicarbonate is made to a very limited extent by a process analogous to the Solvay process (*q. v.*). Trimethylamine is used in place of ammonia because the hydrochloride of the former is much more soluble than ammonium chloride and therefore permits of greater solution concentration with a correspondingly larger yield of the bicarbonate. Potassium chloride is used in place of sodium chloride. The reaction taking place is represented below (5).



**Laboratory Preparation.**—Prepare a saturated solution of potassium carbonate (1 Gm. in 0.9 cc. of water at  $25^\circ\text{ C}$ .) and pass carbon dioxide into the solution until a portion of the liquid does not give an immediate red brown precipitate upon the addition of mercuric chloride test solution (3). Allow the solution to stand for twenty-four hours in a cool place, filter off the crystals and, after washing them with a spray of ice cold water, dry at  $25^\circ\text{ C}$ . in an atmosphere of carbon dioxide.

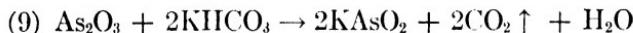
**Pharmaceutical Preparations and Uses.**—1. *Potassium Bicarbonate* (Potassii Bicarbonas), U. S. P. XIII.—Potassium Bicarbonate, when dried for fourteen hours over sulfuric acid, contains not less than 99 per cent of  $\text{KHCO}_3$ . The salt has about the same neutralizing strength as sodium bicarbonate and is more soluble. It is sometimes used as an antacid for gastric hyperacidity (see p. 153) and as a diuretic. Its use as an alkalizer with sulfa therapy (see also p. 154) has been both advocated and opposed. However, it may have a beneficial effect in cases when it is inadvisable to administer sodium bicarbonate (*e. g.*, cardiac edemas) but where sulfa drugs are indicated. The infrequent medicinal use is probably due to the toxic effect of the potassium ion. It is used technically

in the manufacture of baking powder, effervescent salts and as a source of CO<sub>2</sub>. Average dose—unofficial 1 Gm. (approximately 15 grains).

2. *Alkaline Aromatic Solution* (*Liquor Aromaticus Alkalinus*), N. F. VIII.—This solution should contain, in addition to other constituents, 20 Gm. of potassium bicarbonate in 1000 cc. of the solution. (See Sodium Borate, p. 163.) The potassium bicarbonate neutralizes the monobasic acid formed from boric acid and glycerin and forms the potassium salt and an alkaline solution. Undiluted it is used as an antiseptic mouth wash and in a dental spray bottle, diluted with 5 volumes of water.

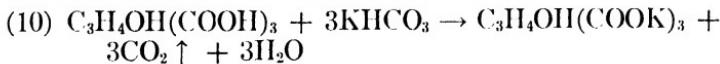
3. *Magnesium Citrate Solution* (*Liquor Magnesii Citratis*), U. S. P. XIII.—Potassium bicarbonate (2.5 Gm.), in addition to other ingredients, is used in preparing 350 cc. of the solution (See also p. 358). It is added to the finished acidic solution just prior to bottling to insure good carbonation of the product. Sodium bicarbonate may replace the potassium salt. Average dose—200 cc. (approximately 7 fluidounces).

4. *Potassium Arsenite Solution* (*Liquor Potassii Arsenitis*, *Fowler's Solution*), U. S. P. XIII.—Potassium Arsenite Solution contains, in each 100 cc., the equivalent of not less than 0.95 Gm. and not more than 1.05 Gm. of As<sub>2</sub>O<sub>3</sub>. The solution is prepared by boiling arsenic trioxide (10 Gm.) and potassium bicarbonate with distilled water (9).



To the reaction mixture, alcohol (30 cc.) and water are added to 1000 cc. It is used as an alterative and tonic (see Arsenic, p. 525). Tenth-normal potassium arsenite (KAsO<sub>2</sub>) is an important reducing agent used in redox (reduction oxidation) volumetric analytical chemistry. It is also used in analyzing iodine preparations. (See U. S. P. XIII, p. 858.) Average dose—0.2 cc. (approximately 3 minimis).

5. *Potassium Citrate Solution* (*Liquor Potassii Citratis*, *Neutral Mixture*), N. F. VIII.—This is a carbonated solution of potassium citrate formed by reacting citric acid (60 Gm.) and potassium bicarbonate (80 Gm.) in distilled water (10).



The potassium bicarbonate supplies the potassium ion and the carbon dioxide. It is used as a diuretic (see p. 225). Average dose—15 cc. (approximately 4 fluidrachms).

## POTASSIUM BITARTRATE

*Potassium Bitartrate*, N. F. VIII



Formula, KHC <sub>4</sub> H <sub>4</sub> O <sub>6</sub> ;	Molecular Weight, 188.18
	CH(OH)COOH

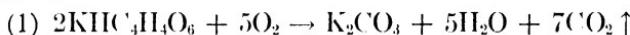
**Physical Properties.**—Potassium Bitartrate occurs as colorless or slightly opaque, rhombic prisms, or as a white, crystalline powder, which is odorless, has a pleasant, acid taste, and is permanent in air. Its density is 1.955.

One Gm. of the salt is soluble in 165 cc. of water and in 8820 cc. of alcohol, at 25° C. One Gm. is soluble in 16 cc. of boiling water.

Potassium bitartrate is soluble in mineral acids, alkalies, and in alkali carbonates. The salt dissolves freely in solutions of boric acid and borax.

**Chemical Properties.**—A saturated aqueous solution of the salt is acid to litmus paper and exhibits the chemical characteristics of the potassium ion (see p. 223).

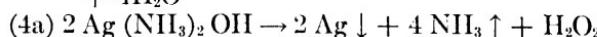
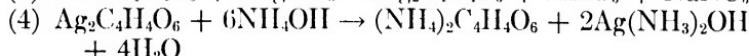
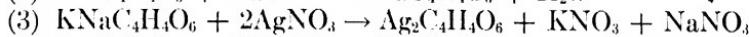
Potassium bitartrate chars when heated and gives off inflammable vapors having the odor of burning sugar. When further ignited at a higher temperature, there remains a white fused mass (1) which gives positive tests for potassium ion and carbonate ion (*q. v.*).



Tartrates when treated with concentrated sulfuric acid char and emit the odor of burning sugar.

Some of the common chemical reactions of the tartrate ion are as follows:

1. When silver nitrate test solution is added to a saturated aqueous solution of potassium bitartrate, previously made neutral with a solution of sodium hydroxide (2), a white precipitate is formed (3). If this precipitate is dissolved in sufficient ammonia test solution (4) and the solution warmed, the silver compound is reduced and metallic silver is deposited on the inner walls of the vessel, forming a mirror (4a).



If the dry salt is treated with a few drops of 1 per cent resorcinol in hydrochloric acid, 3 cc. of sulfuric acid and slowly heated, a rose-red color is formed. This color is destroyed by the addition of water.

When a drop of ferrous sulfate test solution, a few drops of hydrogen peroxide and, finally, an excess of sodium hydroxide test solution are added consecutively to a solution of a tartrate, previously acidified with acetic acid, a purple or violet color is produced.

**Official Tests for Identity.**—1. A solution of the salt is positive to all the tests for the Potassium ion (see p. 223).

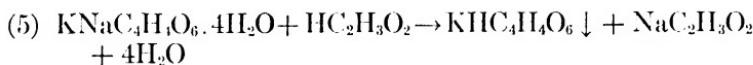
2. Potassium bitartrate chars when heated (*q. v.*).
3. Sodium cobaltic nitrite T.S. forms an orange precipitate with solutions of potassium bitartrate.

4. A silver mirror is formed with silver nitrate T.S. and ammonia T.S. (*q. v.*).

**Commercial Manufacture.**—Potassium bitartrate occurs in many acidulous fruits. It is usually obtained from the juice of grapes. When grape juice in casks is allowed to undergo alcoholic fermentation, crystalline crusts of crude potassium bitartrate known as crude tartar or argol are deposited.

*Argol* is composed of potassium bitartrate, calcium tartrate, coloring materials, extractives, yeast, and other organic substances. The crude tartar is dissolved in boiling water, the solution filtered and then allowed to stand. Slightly colored crystals of potassium bitartrate containing from 5 to 15 per cent of calcium tartrate settle out. These crystals of tartar are boiled with water and most of the coloring matter precipitated by the addition of pipe clay or egg albumen. The solution is filtered through charcoal and crystallized. In order to obtain cream of tartar free from calcium salts, the crystals are dissolved in boiling water, 10 per cent of hydrochloric acid added and the solution stirred continuously while cooling. The crystals of potassium bitartrate are separated from the mother liquor, washed with cold water and dried. An appreciable amount of the bitartrate, together with some tartaric acid, remains in the mother liquor and is frequently utilized in the manufacture of tartaric acid.

Large quantities of cream of tartar of such high purity as to be used medicinally are made by a method known as the "precipitation process." The crude argol from wine casks is dissolved in hot water and partially neutralized with sodium carbonate. The resulting solution is percolated through soda ash, contained in stone cylinders, and the resulting potassium and sodium tartrate purified by crystallization. The slightly colored crystals are then redissolved in water and decomposed by acetic acid into almost pure potassium bitartrate which settles out as a very fine precipitate and sodium acetate which remains in solution (5).



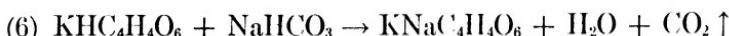
**Laboratory Preparation.**—Dissolve 10 Gm. of potassium and sodium tartrate in 10 cc. of water. Add diluted acetic acid until precipitation ceases. Filter off the white crystalline precipitate of potassium bitartrate, wash it with a small quantity of cold 50 per cent alcohol and dry.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Bitartrate* (Potassii Bitartras, Cream of Tartar, Acid Potassium Tartrate), N. F. VIII.—Potassium Bitartrate, when dried to constant weight at 105° C. for three hours, contains not less than 99.5 per cent of KOOC·CHOH·CHOH COOH.

In doses of from 2 to 8 Gm., potassium bitartrate acts as a diuretic and increases the normal acidity of the urine. In large doses (16 to 30 Gm.) it acts as a laxative. Tartrates, unlike the acetates

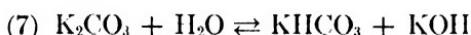
and citrates, are not oxidized in the body to carbonates and therefore do not exhibit an alkalinizing effect. They are less absorbed from the alimentary tract than other salines and therefore cause a laxative action.

Potassium bitartrate has recently been suggested to replace talc as a dusting powder in surgery.<sup>1,2</sup> It is more bacteriostatic and more readily absorbed than talc. In the industries it is used as a reducer of CrO<sub>3</sub> in a mordant bath for wool dyeing; in mixtures of chalk and alum as a silver cleaner; for coloring metals; and in baking powders to raise the dough (6).

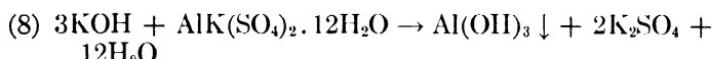


Average dose --2 Gm. (approximately 30 grains).

2. *Cochineal Solution* (Liquor Coccii, Cochineal Color), N. F. VIII.—The cochineal used in this preparation contains carminic acid which is thought to be partly responsible for the coloring properties. In preparing this solution the cochineal (65 Gm.) is triturated with potassium carbonate (32 Gm.), and to this is added water (500 cc.) (7).



Alum is dissolved in the aqueous mixture with slow stirring (8).



The alkaline potassium carbonate causes the precipitation of aluminum hydroxide which reacts with the cochineal and carminic acid, to form an aluminum "lake" which absorbs the coloring matter. The addition of potassium bitartrate (65 Gm.), which is acidic, dissolves that portion of the aluminum lake which is soluble in a boiling acid media. Glycerin (450 cc.) is added as a preservative, the mixture filtered and made up to 1000 cc. with distilled water. This solution imparts a brilliant red color.<sup>3</sup> preparations and since it is stable in acid media is used for coloring this type of product. Carmine solution is an alkaline preparation of carmine, the aluminum lake obtained from cochineal. It has a deep red color and is used for coloring alkaline pharmaceuticals. Acids cause a precipitate to form.

3. *Compound Jalap Powder* (Pulvis Jalapæ Compositus, Pulvis Purgans), N. F. VIII.—This powder is a mixture of Jalap (350 Gm.) and Potassium Bitartrate (650 Gm.). Jalap is employed as a purgative in chronic constipation where the bowel contains hard fecal masses. It is often prescribed with extract of belladonna or hyoscyamus, or with a little carminative oil to prevent the pain and griping effect. Potassium bitartrate also relieves the harsh action

<sup>1</sup> Am. Prof. Pharm., 10, 839 (1944).

<sup>2</sup> J. Am. Med. Assn., 126, 236 (1944).

of Jalap and being a saline laxative, helps supply fluid to the bowel. Average dose—2 Gm. (approximately 30 grains).

## POTASSIUM BROMIDE

*Potassium Bromide*, U. S. P. XIII

Formula, KBr. Molecular Weight, 119.01

**Physical Properties.**—Potassium Bromide occurs as colorless, translucent, or white cubical crystals, or as a granular powder. It is odorless and has a sharp, saline taste. The salt is stable in air and has a specific gravity of 2.75 at  $\frac{2}{4}^{\circ}$ .

One Gm. of the salt is soluble in 1.5 cc. of water, in 250 cc. of alcohol, and in 5 cc. of glycerin, at  $25^{\circ}$  C. It is soluble in 1 part of boiling water and in about 21 parts of boiling alcohol.

When potassium bromide is heated it decrepitates, and at about  $730^{\circ}$  C. it fuses without decomposing. At a bright red heat (about  $1435^{\circ}$  C.), it volatilizes.

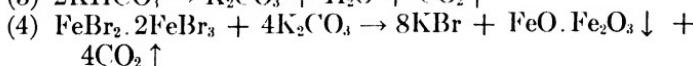
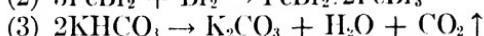
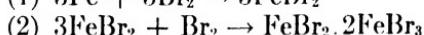
**Chemical Properties.**—Aqueous solutions of potassium bromide are neutral or faintly alkaline to litmus paper. The bromide ion forms insoluble salts with silver, mercurous mercury and lead.

**Official Tests for Identity.**—1. An aqueous solution of potassium bromide responds to all tests for *Potassium* ion (*q. v.*).

2. The tests and chemistry of the bromide ion are discussed with Sodium Bromide, p. 140.

**Commercial Manufacture.**—The bromides of the alkali metals are all prepared by the same process. (See Sodium Bromide, p. 164.)

**Laboratory Preparation.**—When bromine is added to iron wire, ferrous bromide is formed (1) which, upon treatment with potassium carbonate, yields potassium bromide and ferrous carbonate (greenish-brown). When the mixture is boiled, the latter changes to ferrous and ferric hydroxides, which may be filtered off. If, however, the bromine is added in two portions (as directed), a ferrous-ferric bromide is produced (2) which, when treated with the alkaline carbonate (3) yields potassium bromide and the ferroso-ferric oxide (4). The latter is much easier to wash free from potassium bromide than the hydroxide.

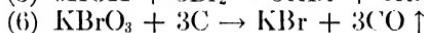
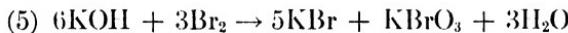


**Method 1.**—Place 5 Gm. of iron wire in a 250-cc. flask and cover it with 50 cc. of distilled water. Add 9 Gm. of bromine in small portions at a time, shaking the flask after each addition and allowing the reaction to cease before adding more bromine. If the solution is still reddish brown after the addition of the bromine, warm gently

until a green solution results. Filter off the excess iron and to the filtrate add 3 Gm. more of bromine and shake well.

Dissolve 15 Gm. of potassium bicarbonate in 50 cc. of distilled water and boil the solution until all carbon dioxide is driven off. Add the solution of the iron bromides to the hot solution of potassium carbonate and continue the boiling for fifteen minutes. The solution at this point should be alkaline; if not, more potassium carbonate should be added and the heating continued. Let the precipitate subside, filter, and wash with hot water. Concentrate the filtrate and allow the salt to crystallize.

*Method 2.*—Gradually add bromine to 125 cc. of a 5 per cent solution of potassium hydroxide contained in a flask until a permanent, brownish color is obtained (about 10 Gm. of bromine required). Agitate the solution constantly during the addition (5). Evaporate the liquid to dryness under a hood and powder the residue. Then mix it with 10 Gm. of finely powdered wood charcoal and heat to a dull red heat in an iron crucible (6). Pour out the fused contents and allow to cool. Dissolve in boiling water, filter and crystallize.



**Pharmaceutical Preparations and Uses.**—1. *Potassium Bromide* (Potassii Bromidum), U. S. P. XIII.—Potassium Bromide, when dried to constant weight at 110° C. for four hours, contains not less than 99 per cent of KBr.

The bromide ion is responsible for the physiological effect produced by potassium bromide (see p. 91). When associated with potassium ion, the combination is very effective. A large dose of potassium bromide has a definite action upon the heart. This is occasioned entirely by the potassium ion. Potassium bromide is usually employed in cases of mental excitement and all conditions arising therefrom, *e. g.*, insomnia, nervousness, etc. It is of particular value in controlling the seizures of epilepsy. It is a good sedative but possesses no anodyne properties. Average dose—1 Gm. (approximately 15 grains).

2. *Five Bromides Elixir* (Elixir Bromidorum Quinque), N. F. VIII.—In addition to other ingredients, this elixir should contain 70 Gm. of potassium bromide in 1000 cc. (See p. 166.) Average dose—4 cc. (approximately 1 fluidrachm).

3. *Three Bromides Elixir* (Elixir Bromidorum Trium), N. F. VIII.—This elixir should contain, besides other ingredients, 80 Gm. of potassium bromide in 1000 cc. (See p. 116.) Average dose—4 cc. (approximately 1 fluidrachm).

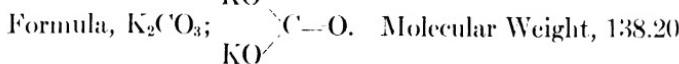
4. *Bromides Syrup* (Syrupus Bromidorum), N. F. VIII.—This elixir contains 8 Gm. of potassium bromide in addition to other ingredients in each 100 cc. (See p. 116.) Average dose—4 cc. (approximately 1 fluiddrachm).

5. *Three Bromides Tablets* (Tabellæ Bromidorum Trium, Triple Bromide Tablets), N. F. VIII.—(See p. 166.)

6. *Potassium Bromide Elixir* (*Elixir Potassii Bromidi*), N. F. VIII.—This elixir contains 175 Gm. of potassium bromide, dissolved in sufficient distilled water, syrup and aromatic elixir to make 1000 cc. Average dose—4 cc. (approximately 1 fluidrachm).

### POTASSIUM CARBONATE

*Potassium Carbonate*, U. S. P. XIII



**Physical Properties.** Potassium Carbonate is a white, granular powder. It is odorless and has a strong alkaline taste. It rapidly absorbs moisture from the air and forms an oily solution ("Oleum Tartari"). Crude potassium carbonate occurs in lumps or as a coarse granular powder, the color ranging from grayish-white to reddish-brown, depending upon the amount of iron present. The anhydrous salt has a specific gravity of 2.29 at  $25^{\circ}\text{C}$ .

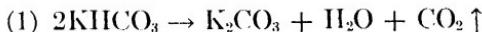
One Gm. of the official salt is soluble in 1 cc. of water at  $25^{\circ}\text{C}$ . and in about 0.7 cc. of boiling water. It is soluble in glycerin but insoluble in alcohol.

Potassium carbonate crystallizes from aqueous solutions in monoclinic crystals,  $\text{K}_2\text{CO}_3 \cdot 3\text{H}_2\text{O}$ , which lose water at  $100^{\circ}\text{C}$ ., giving a white powder,  $\text{K}_2\text{CO}_3 \cdot 1\frac{1}{2}\text{H}_2\text{O}$ .

When heated to  $125^{\circ}\text{C}$ ., the salt begins to lose adhering water (which should not be less than 10 per cent and not more than 16.5 per cent in the official salt) and at  $180^{\circ}\text{C}$ . all water is expelled. At  $891^{\circ}\text{C}$ . the salt melts, and slowly volatilizes as the temperature is increased to that of white heat.

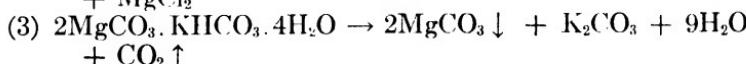
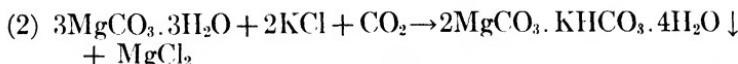
**Chemical Properties.**—The important chemical properties are due to the carbonate ion and these are discussed with Sodium Carbonate, page 167.

A very pure salt may be made by heating crystallized potassium bicarbonate to about  $190^{\circ}\text{C}$ . Carbon dioxide and water are expelled and a carbonate of U. S. Pharmacopœial purity remains (1).



**Official Tests for Identity.**—1. Potassium carbonate or its solutions respond to the tests for *potassium* ion (*q. v.*) and *carbonate* ion. (See p. 167.)

**Commercial Manufacture.**—1. In the most recent method, a cold slurry of concentrated potassium chloride and tri-hydrated magnesium carbonate, is treated with  $\text{CO}_2$  (2). The double salt that results is filtered off, washed and decomposed (3).



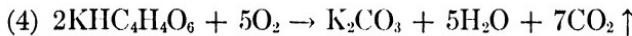
2. The salt is prepared from potassium chloride and potassium sulfate by a method similar to the Le Blanc process for the manufacture of sodium carbonate (*q. v.*).

Other sources of potassium carbonate are wood ashes, the sugar-beet industry and potassium bitartrate.

3. Wood ashes are lixiviated in wooden tubs, the solution evaporated to dryness in iron pots, and the residue calcined in a reverberatory furnace. The crude "potashes" so obtained contain potassium carbonate, varying amounts of sulfate and chloride and insoluble matter (silicates).

4. Potassium carbonate of such purity as to warrant its use as "pearlash" is made by calcining the residue left after distilling beet root spirit, made by the fermentation of molasses from beet root sugar.

5. At one time potassium carbonate was prepared by calcining pure potassium bitartrate (cream of tartar) from which it gets the name "salt of tartar" (4). The product of the calcination was composed of a mixture of potassium carbonate and charcoal, from which the former was extracted by lixiviation with water. The solution was filtered and evaporated to dryness in iron or platinum vessels and the residue fully dehydrated by gentle ignition.



**Laboratory Preparation.**—Mix 10 Gm. of pure powdered potassium bitartrate with 5 Gm. of powdered potassium nitrate. Ignite the mixture. When the reaction has ceased, place the residue in a porcelain crucible and heat at dull redness for several hours. When the residue is nearly white, allow it to cool and dissolve in a small quantity of water. Filter, concentrate the solution, and granulate the salt.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Carbonate* (Potassii Carbonas), U. S. P. XIII.—Potassium Carbonate, when dried to constant weight at 180° C., contains not less than 99 per cent of  $\text{K}_2\text{CO}_3$ . It contains not less than 10 per cent and not more than 16.5 per cent of water. Potassium carbonate may be used for the same medicinal purposes as the bicarbonate but, on account of its decided alkaline reaction, it is rarely employed. When taken internally in large doses it produces gastric irritation of sufficient severity to cause death. The important uses are in pharmaceutical preparations where its alkaline property is of value.

2. *Alkaline Rhubarb Elixir* (Elixir Rhei Alkalimum, Neutralizing Cordial), N. F. VIII.—Potassium carbonate (16 Gm. in 1000 cc.) is present to neutralize the tannic acid in the rhubarb and thus reduce the astringent tendency. It is used as an antacid and anti-diarrheal. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Cochineal Solution* (Liquor Coccii, Cochineal Color), N. F. VIII.—In addition to other ingredients, Cochineal Color contains 32 Gm. of potassium carbonate in 1000 cc. The presence of the

alkaline potassium carbonate produces hydroxyl ions necessary to form aluminum hydroxide. (See Potassium Bitartrate, p. 232.)

4. *Carminative Mixture* (*Mistura Carminativa*, *Dalby's Carminative*), N. F. VIII.—Potassium carbonate (3 Gm. in 1000 cc.) is not present in a sufficient quantity to contribute much to the therapeutic value of this preparation. It does provide antacid properties. Carminative Mixture is used as a carminative and anti-diarrheal for small children. Average dose—for infants, 0.5 cc. (approximately 8 minims).

5. *Ferrous Carbonate Pills* (*Pilulae Ferri Carbonatis*, *Chalybeate Pills*, *Blaud's Pills*, *Ferruginous Pills*), N. F. VIII.—Potassium carbonate supplies the carbonate ion for the formation of ferrous carbonate (5).



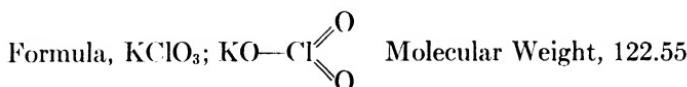
6. *Alkaline Sulfur Ointment* (*Unguentum Sulfuris Alkalimum*), N. F. VIII.—When sulfur in an ointment base is applied to the skin, some of it appears to be converted into sulfide (see p. 564). The sulfide is effective in destroying some parasites such as those causing ring-worm, scabies and pediculosis. The addition of potassium carbonate (10 per cent) increases the amount of sulfide formed and increases the effectiveness of the sulfur ointment. Alkali present in the ointment increases the penetrating power by softening the epidermis of the skin. This allows the entrance of sulfur into the deep burrows.

7. *Aromatic Rhubarb Syrup* (*Syrupus Rhei Aromaticus*), U. S. P. XIII.—A small amount of potassium carbonate (1 Gm. per 1000 cc.) is used to prevent the syrup from becoming turbid. The aromatic rhubarb tincture contains resins and volatile oils which react with the potassium carbonate to form water-soluble compounds. This syrup is used as an astringent laxative for infants. Average dose—10 cc. (approximately 2½ fluidrachms).

8. *Rhubarb Syrup* (*Syrupus Rhei*), N. F. VIII.—The alkaline potassium carbonate prevents the precipitation of the rhubarb resin when the fluidextract (alcoholic) is diluted with syrup (aqueous). It is used as a laxative. Average dose—10 cc. (approximately 2½ fluidrachms).

## POTASSIUM CHLORATE

### *Potassium Chlorate*, N. F. VIII



**Physical Properties.**—Potassium chlorate was first prepared by Berthollet in 1786. It occurs as colorless, lustrous, monoclinic prisms or plates, or as a white, granular powder. It is odorless, and has a characteristic cooling taste. It has a specific gravity of 2.32 ( $\frac{29}{4}^{\circ}\text{C}.$ ). The salt is stable in air.

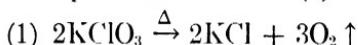
One Gm. of potassium chlorate is soluble in 16.5 cc. of water at 25° C. and in about 1.8 cc. of boiling water. It is almost insoluble in 95 per cent alcohol, but is slightly soluble in hydroalcoholic solutions. The salt dissolves readily in glycerin.

When the salt is heated to about 360° C. it melts, and decomposes into oxygen and potassium chloride.

**Chemical Properties.**—Potassium chlorate decomposes with explosive violence when it is heated or subjected to concussion. It also decomposes suddenly (dangerous) when triturated with organic substances, *e. g.*, cork, tannic acid, dust, sucrose, etc., or with phosphorus, sulfur, sulfides, hypophosphites, charcoal, reduced iron, or other easily oxidizable substances. An aqueous solution is neutral to litmus paper.

Potassium chlorate exhibits certain reactions that are characteristic of all chlorates.

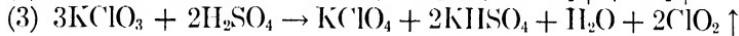
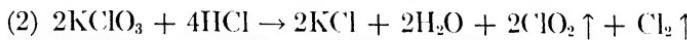
1. A solution of the salt does not give a precipitate with silver nitrate. Upon heating dry chlorate, oxygen is given off and the residue is potassium chloride (1).



Potassium chloride dissolved in water gives the characteristic chloride ion test and responds to all tests for potassium ion.

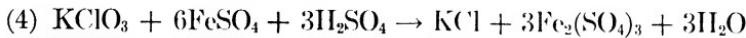
2. If a solution of potassium chlorate and sulfuric acid is added to an indigo solution, and then a few drops of sodium sulfite solution added, the color of the indigo is destroyed. Chlorates react with acids to produce unstable chlorine dioxide ( $\text{ClO}_2$ ). (See Chlorine, p. 88.) The sulfurous acid formed reduces the chlorate to a lower oxide of chlorine. The chlorine oxides have strong bleaching properties.

3. When a very little potassium chlorate is treated with hydrochloric or sulfuric acid in a test-tube it turns greenish to orange-yellow, and chlorine and oxides of chlorine are evolved (2) (3).



When heat is applied there is a crackling noise, due to explosions of the  $\text{ClO}_2$ .

4. Potassium chlorate is a strong oxidizing agent and, therefore, reacts readily with reducing agents (4) (5).

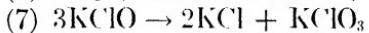
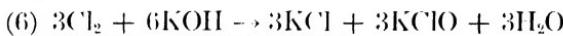


**Official Tests for Identity.**—1. Potassium chlorate when heated to 400° C. gives off oxygen and finally leaves a residue of potassium chloride (*q. v.*), which is readily soluble in water and which responds to the tests for *Potassium* ion, page 223, and for *Chloride* ion, page 109.

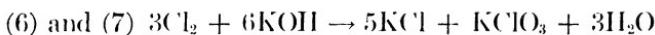
2. Potassium chlorate (0.2 Gm.) added to 1 cc. of hydrochloric acid produces chlorine and chlorine dioxide (*q. v.*).

**Commercial Manufacture.**—1. Nearly all potassium chlorate is made by the electrolysis of warm, alkaline solutions of potassium chloride. The electrolytic process was first used in Switzerland in 1891. At present it is used extensively both in Europe and in the United States (Niagara Falls, etc.). When warm aqueous solutions of potassium chloride are subjected to an electric current, chlorine collects at the anode and potassium hydroxide together with hydrogen is formed at the cathode. If a single cell is used, the solution is circulated so as to bring the potassium hydroxide in contact with the chlorine. Potassium chlorate is formed and crystallizes out. If a number of cell units are employed, the anodes and cathodes are separated by porous diaphragms and the solution of potassium hydroxide is carried by a process of circulation to the anode compartment of the next cell, where potassium chlorate is formed and crystallizes out.

2. When chlorine is passed into a *warm*, concentrated (90 per cent) solution of potassium hydroxide, potassium hypochlorite is formed (6). In the presence of an excess of chlorine, potassium hypochlorite changes into potassium chlorate as fast as it is produced (7).

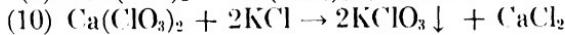
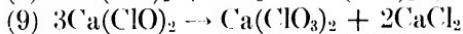
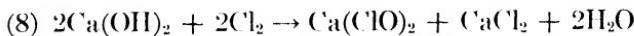


or



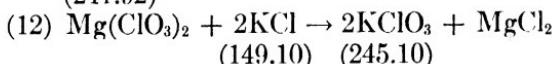
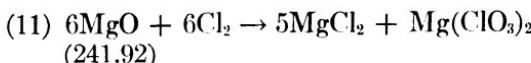
This process is seldom, if ever, used commercially because it involves the conversion of about 83 per cent of the valuable potassium hydroxide into the relatively less valuable potassium chloride. However, manufacturers sometimes prepare the salt by an analogous reaction, using milk of lime. The process is described below.

3. Milk of lime is treated with an excess of chlorine in a vessel in which the mixture is constantly stirred (8). A suspension of magnesium oxide is said to be preferable to milk of lime because the resulting magnesium chloride has a lesser solvent action than calcium chloride upon the potassium chlorate. When the chlorination is complete the mixture is allowed to settle (8 and 9), the clear supernatant liquid is drawn off, mixed with potassium chloride, and evaporated to a specific gravity of 1.28. At this concentration potassium chloride reacts with calcium chlorate to form potassium chlorate (10) which, because of its lesser solubility in water, crystallizes out. It is purified by recrystallization from hot water.



**Laboratory Preparation** - Suspend 25 Gm. of magnesium oxide in 150 cc. of water and warm to 40° C. Slowly pass chlorine into the suspension, which is constantly stirred, until it is saturated (11). Then allow the mixture to settle, decant the clear, supernatant

liquid, and mix it with 15 Gm. of potassium chloride (12). Evaporate the solution on a water-bath to a specific gravity of 1.28 and allow it to cool. On account of the relative insolubility of the potassium chlorate in cold water, this salt crystallizes out. It may be recrystallized from hot water.



**Pharmaceutical Preparations and Uses.**—1. *Potassium Chlorate* (*Potassii Chloras*), N. F. VIII.—Potassium chlorate contains not less than 99 per cent of  $\text{KClO}_3$ .

*Great caution should be observed in handling this salt, as dangerous explosions are liable to occur when it is heated or subjected to concussion, or to trituration with organic substance, such as cork, tannic acid, dust, sucrose, etc., or with charcoal, sulfur, sulfides, hypophosphites, reduced iron, or other easily oxidizable substances.*

Because of its oxidizing power potassium chlorate was introduced into medicine as an oxidizing germicide. The killing effect against bacteria, however, has been found to be no more than that of inert salts. When the salt is taken orally and absorbed it causes lysis of red blood corpuscles, and the protein débris liberated by this destruction irritates the kidney and produces a very marked interstitial nephritis, due to blocking of the vessels. It is usually used in the form of a gargle or mouth wash. Patients should be cautioned against swallowing the solution. The salt is used in some tooth pastes. Potassium chlorate is employed in the manufacture of pyrotechnics, matches, and dyes.

2. *Potassium Chlorate Gargle With Iron* (*Gargarisma Potassii Chloratis cum Ferro*, Golden Gargle), N. F. VIII.—Ferric chloride tincture (120 cc.) is added to a solution of potassium chlorate (45 Gm.) in glycerin (240 cc.) and distilled water (*q. s.*, 1000 cc.).

3. *Potassium Chlorate Tablets* (*Tabellæ Potassii Chloratis*), N. F. VIII.—These tablets contain not less than 94 per cent and not more than 106 per cent of the labeled amount of  $\text{KClO}_3$ . The internal use is very dangerous and it is rarely so employed. Average dose—0.3 Gm. (approximately 5 grains).

## POTASSIUM CHLORIDE

*Potassium Chloride*, U. S. P. XIII

Formula,  $\text{KCl}$ . Molecular Weight, 74.55

**Physical Properties.**—Potassium Chloride occurs in the form of colorless, elongated, prismatic, or cubical crystals, or as a white, granular powder. The salt is odorless and possesses a saline taste. It is permanent in air. It has a specific gravity of 1.988 ( $\frac{20}{4}$ °), and

melts at 772° C. When heated it decrepitates, and upon prolonged heating at red heat it sublimes.

One Gm. of Potassium Chloride dissolves in 2.8 cc. of water at 25° C., and in about 2 cc. of boiling water. It is insoluble in alcohol and ether.

**Chemical Properties.**—The chloride ion is responsible for the important chemical properties (see p. 109). A 10 per cent aqueous solution of potassium chloride is neutral to litmus paper.

**Official Tests for Identity.**—1. A solution of potassium chloride gives all of the tests for potassium ion (*q. v.*).

2. Potassium chloride solutions also respond to all of the tests for chloride ion (see p. 174).

**Commercial Manufacture.**—The sources of potassium chloride are: (1) *carnallite*, (2) *sylvinit*e, and (3) a bed of solid salt of very complex composition found at *Searles Lake*.

1. *Carnallite* ( $MgCl_2 \cdot KCl \cdot 6H_2O$ ) which contains potassium equivalent to 26 per cent  $K_2O$ , is found in extensive deposits in Stassfurt, Germany. In these deposits with carnallite (55 per cent) are found sodium chloride (25 per cent) and *pieserite* ( $MgSO_4 \cdot H_2O$ ) (15 per cent). The removal of the potassium chloride is complicated by the presence of the other salts. A process of fractional crystallization is carried out whereby the raw salt deposit is ground up and treated with hot water. The hot solution is allowed to stand until the insoluble material settles, transferred to clean containers and then allowed to cool causing about 80 per cent of the potassium chloride to crystallize. The process is repeated using the mother liquor and wash water.

2. *Sylvinit*e is found in large deposits in Alsace-Lorraine and near Carlsbad, New Mexico. It is a mixture of sodium and potassium chlorides. Two methods are used to separate these chlorides: (a) Crystallization, and (b) Flotation.

(a) *Crystallization Process.*—The sylvinit is crushed and extracted with hot water at the boiling point (110° C.). The hot solution is filtered and cooled by flask evaporation in vacuum crystallizers. The rapid cooling by the removal of water tends to cause both potassium and sodium chloride to crystallize out. The sodium chloride is prevented from separating out by the simultaneous addition of water corresponding to the quantity evaporated off. This is due to the fact that sodium chloride has about the same solubility in cold water as in hot water (2.8 per cent in cold and 2.7 per cent in boiling water) whereas the cooled solution is filtered and the crystals of potassium chloride recovered. The mother liquor is reheated and used over only this time it will dissolve only the potassium chloride from the sylvinit since it is already saturated with sodium chloride.

(b) *Flotation Process.*—The chlorides of potassium and sodium exist in sylvinit as a mechanical mixture and not as a double salt or as mixed crystals. When the crude ore is crushed to about 40 mesh, the crystalline form of both potassium and sodium chloride

separate out. A special flotation agent has been found that carries off the sodium chloride in the froth and allows the potassium chloride to collect on the bottom of the apparatus.

3. *Searles Lake* is the location of a deposit of salts consisting of K, Na, Cl, CO<sub>3</sub>, B<sub>4</sub>O<sub>7</sub>, PO<sub>4</sub>, and other ions in small amounts. A brine is present that is pumped into evaporators and by a series of evaporation and fractional crystallizations the salts present are separated.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Chloride* (Potassii Chloridum), U. S. P. XIII.—Potassium chloride, when dried for two hours at 110° C., contains not less than 99 per cent of KCl. Potassium chloride has been known for a long time as an effective diuretic. It has also been used successfully in the treatment of Ménière's disease, myasthenia gravis, and familial periodic paralysis. More recently its use has been suggested for the relief of allergic symptoms including urticaria, hay fever, asthma, sinusitis of allergic origin, and migraine.

Sullivan,<sup>1</sup> in 1941, explained this use in allergy by pointing out that the parasympathetic nervous system dominates the sympathetic and causes water imbalance. Potassium and calcium salts are supposed to reestablish autonomic nervous system balance.

2. *Potassium Chloride Tablets* (Tabellæ Potassii Chloridi), U. S. P. XIII.—Potassium Chloride Tablets contain not less than 95 per cent and not more than 105 per cent of the labeled amount of KCl. Average dose—1 Gm. (approximately 15 grains).

3. *Ringer's Solution* (Liquor Ringeri, Isotonic Solution of Three Chlorides, U. S. P. XII), U. S. P. XIII.—Ringer's Solution contains, in each 100 cc., not less than 25 mg. and not more than 35 mg. of KCl, and the salts NaCl and CaCl<sub>2</sub>.2H<sub>2</sub>O. (See Sodium Chloride, p. 178.)

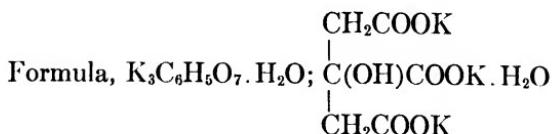
4. *Lactated Ringer's Solution* (Liquor Ringeri Lacticus), U. S. P. XIII.—Lactated Ringer's Solution is a sterile solution in water for injection containing, in each 100 cc., not less than 27 mg. and not more than 33 mg. of KCl, and the salts CaCl<sub>2</sub>.2H<sub>2</sub>O, NaCl and NaC<sub>3</sub>H<sub>5</sub>O<sub>3</sub>. (See Sodium Chloride, p. 178.)

5. *Pectin Paste* (Pasta Pectini), N. F. VIII.—This product contains potassium chloride as a constituent of the Ringer's Solution used in its preparation.

6. *Thin Pectin Paste* (Pasta Pectini Tenuis), N. F. VIII.—Potassium chloride is present in the Ringer's Solution used.

### POTASSIUM CITRATE

*Potassium Citrate*, U. S. P. XIII



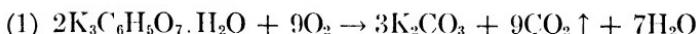
Molecular Weight, 324.40

<sup>1</sup> J. Missouri Med. Assn., 38, 125 (1941).

**Physical Properties.**—Potassium Citrate occurs in colorless, prismatic crystals, or as a white, granular powder. It is odorless, and has a cooling, saline taste. It has a specific gravity of 1.906 at  $\frac{2}{4}^{\circ}$ . The salt is deliquescent in moist air and, therefore, should be kept in air-tight containers.

One Gm. of the salt dissolves in 1 cc. of water at  $25^{\circ}$  C. It is freely soluble in glycerin but almost insoluble in alcohol.

**Chemical Properties.**—When heated to  $100^{\circ}$  C., the salt begins to lose water and at about  $200^{\circ}$  C. it becomes anhydrous. The anhydrous salt has a density of 1.908 and crystallizes in the triclinic system. At higher temperatures it carbonizes and emits inflammable gases having a pungent, acrid odor. A residue of carbon and potassium carbonate remains (1).

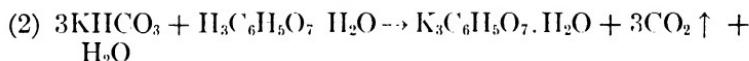


An aqueous solution is alkaline to litmus paper (see p. 181).

**Official Tests for Identity.**—1. A solution of potassium citrate responds to the tests for Potassium ion (see p. 224).

2. An aqueous solution also gives the tests for the *Citrate* ion (see p. 182).

**Commercial Manufacture.**—Potassium citrate is prepared by neutralizing a solution of citric acid with potassium carbonate or bicarbonate (2). The solution is evaporated either to crystallization or to dryness with constant stirring. The resulting granular mass obtained by the latter process is reduced to a uniform fine powder by trituration in a warm mortar.



**Laboratory Manufacture.**—Prepare the salt in the laboratory by dissolving 10 Gm. of citric acid in 50 cc. of distilled water and adding small quantities of potassium bicarbonate to the solution contained in an evaporating dish, until effervescence ceases. The solution is evaporated on a water-bath and granulated in the usual way.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Citrate* (Potassii Citras), U. S. P. XIII.—Potassium citrate, when rendered anhydrous by drying at  $180^{\circ}$  C., contains not less than 90 per cent of  $\text{C}_3\text{H}_4\cdot\text{OH}\cdot(\text{COOK})_3$ . It contains not less than 3 per cent and not more than 6 per cent of water. The diuretic, expectorant and diaphoretic actions are greater than the other alkaline salts and the compounds of ammonia. This salt has a laxative action due to the salt action and to slow absorption. Any expectorant action is probably empirical since the intake of water is also beneficial. It functions as a systemic alkalinizing agent in the same manner as other alkali salts of organic acids (see p. 183). Average dose—1 Gm. (approximately 15 grains).

2. *Effervescent Potassium Citrate* (Potassii Citras Effervescens), U. S. P. XIII.—This preparation contains potassium citrate (200 Gm.), sodium bicarbonate (477 Gm.), tartaric acid (252 Gm.) and citric acid (162 Gm.) to make 1000 Gm. It is used primarily

for the effects of potassium citrate but exerts also a laxative action because of the sodium tartrate formed (see p. 209). Average dose—4 Gm. (approximately 60 grains).

3. *Potassium Citrate Solution* (*Liquor Potassii Citratis*), N. F. VIII.—This solution "is an aqueous solution containing, in each 100 cc., not less than 8 Gm. of  $C_3H_4.OH.(COOK)_3$ , with small amounts of free citric and carbonic acids." Solutions of potassium bicarbonate and citric acid are mixed and when effervescence ceases the resulting product is bottled and stoppered tightly. To insure proper carbonation and a palatable preparation it must not be dispensed unless it has been recently prepared. It is used as a diuretic. Average dose—15 cc. (approximately 4 fluidrachms).

### POTASSIUM HYDROXIDE

*Potassium Hydroxide*, U. S. P. XIII

Formula, KOH. Molecular Weight, 56.10

**Physical Properties.**—Potassium Hydroxide is obtainable in dry, hard, brittle, white or nearly white, sticks, in fused masses, in small pellets, in flakes, and in other forms that have a crystalline fracture and a density of 2.044. It is very deliquescent and rapidly absorbs both moisture and carbon dioxide from the air. Potassium hydroxide and its solutions rapidly destroy organic tissues and form a slimy mass by decomposition of the proteins. Therefore, great care should be exercised in handling it.

One Gm. of Potassium Hydroxide dissolves in 1 cc. of water, in about 3 cc. of alcohol, and in about 2.5 cc. of glycerin, at 25° C. One Gm. is soluble in 0.6 cc. of boiling water. It is very soluble in boiling alcohol.

At 360° C. the base fuses. At higher temperatures, it is appreciably volatilized.

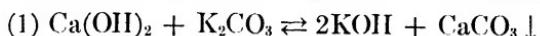
**Chemical Properties.**—The chemical properties of potassium hydroxide are due entirely to its basic character and high degree of ionization. The chemical characteristics of potassium hydroxide are the same as those of sodium hydroxide (see p. 188). For reactions of the potassium ion see p. 223.

**Official Tests for Identity.**—1. All solutions of potassium hydroxide, even when greatly diluted, are strongly alkaline to litmus paper, phenolphthalein test solution, etc.

2. It responds to all reactions for potassium ion (*q. v.*).

**Commercial Manufacture.**—Potassium hydroxide is manufactured in two ways: (1) by causticizing potassium carbonate with milk of lime and (2) by the electrolysis of a solution of potassium chloride.

*Process 1.*—Attention has been called to the fact that potassium hydroxide is the principal commercial product of the reaction between calcium hydrate and potassium carbonate (1).



*Process 2.*—The electrolytic process is by far the simpler of the two for manufacturing potassium hydroxide. When a direct current is

passed through a solution of potassium chloride in a diaphragm cell, chlorine is liberated at the anode and potassium hydroxide together with hydrogen is formed at the cathode. (See Sodium Hydroxide, p. 190.)

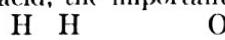
**Laboratory Preparation of Potassium Hydroxide Solution.**—Dissolve 6 Gm. of anhydrous potassium carbonate in 60 cc. of boiling water. Gradually add 5 Gm. of calcium hydroxide (freshly slaked lime) and boil the mixture until a few drops of the filtered liquid give no effervescence with diluted hydrochloric acid. If, after boiling for fifteen minutes, the caustic liquor still gives a test for carbonates, add more calcium hydroxide and again boil, in each case replacing the water lost by evaporation. When the causticization is complete, allow the precipitate to subside, decant the supernatant liquid and filter through asbestos on a Gooch crucible, washing the precipitate with sufficient hot water to bring the final volume of the caustic liquor up to 100 cc. (1).

The volume of the boiling liquor should never become less than 60 cc. because, in concentrated solutions, any potassium hydroxide formed will react with the calcium carbonate to form potassium carbonate and calcium hydroxide.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Hydroxide* (Potassii Hydroxidum, Caustic Potash), U. S. P. XIII.—Potassium Hydroxide contains not less than 85 per cent of total alkali, calculated as KOH, of which not more than 3.5 per cent is  $K_2CO_3$ . *Caution.*—*Great care is necessary in handling Potassium Hydroxide, as it rapidly destroys organic tissues.* Because of its escharotic properties it finds little use as such in therapeutics. The principal use is in chemical and pharmaceutical processes and particularly those in which the potassium ion is desired, *i. e.*, soft soap manufacture. It is rarely used internally and to some extent externally as a cauterizing agent. In analytical chemistry it finds some use as an alkaline reagent.

2. *Saponated Cresol Solution* (Liquor Cresolis Saponatus, Compound Cresol Solution), U. S. P. XIII.—This solution consists essentially of cresol dissolved in a soap, the soap being formed by the saponification (see p. 189) of a vegetable oil with potassium or sodium hydroxide (see p. 189). It is used as a general disinfectant.

3. *Medicinal Soft Soap* (Sapo Mollis Medicinalis, Soft Soap, Green Soap), U. S. P. XIII.—This is a potassium soap made by the saponification (see p. 189) of vegetable oils, excluding coconut oil and palm kernel oil, without the removal of glycerin. Since the chief constituent of vegetable oils is olein which upon saponification yields glycerin and oleic acid, the important soap present is



potassium oleate ( $\text{CH}_3-\text{[CH}_2]_7-\text{C}(\text{H})=\text{C}(\text{H})-\text{[CH}_2]_7-\text{C}(\text{O}-\text{K})$ ).

4. *Soft Soap Liniment* (Linimentum Saponis Mollis, Tincture of Green Soap), U. S. P. XIII.—This preparation uses potassium hydroxide indirectly in that medicinal soft soap is the main ingredient.

5 *Soda Lime* (Calx Soda), U. S. P. XIII.—This product is a mixture of calcium hydroxide with sodium or potassium hydroxide or both, intended for use in metabolism tests, anesthesia, and oxygen therapy. (See Sodium Hydroxide, p. 192.)

6. *Potassium Hydroxide Solution* (Liquor Potassii Hydroxidi), N. F. VIII.—This solution contains, in each 100 cc., not less than 4.5 Gm. and not more than 5.5 Gm. of total alkali, calculated as KOH, of which not more than 0.35 Gm. is  $K_2CO_3$ . Potassium hydroxide is only 85 per cent KOH, and therefore 60 Gm. is used to make 1000 cc. The solution must be stored in a tightly stoppered bottle to prevent absorption of carbon dioxide from the air. If this were not done, on long standing the  $K_2CO_3$  content would increase as the KOH content decreased. The stopper should be made of rubber and the bottle of hard glass. A glass stopper is liable to "freeze" in the neck of the bottle. The use of a little petrolatum on the glass stopper helps prevent "freezing." Because the solution is strongly alkaline it is necessary to use glass wool or asbestos as a filter.

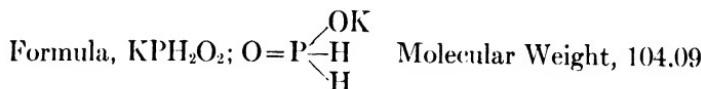
*Caution.*—*Potassium Hydroxide Solution should be freely diluted with water before being taken into the mouth.* Average dose—1 cc. (approximately 15 minimis).

7. *Aromatic Eriodictyon Syrup* (Syrpus Eriodictyi Aromaticus, Aromatic Yerba Santa Syrup, Syrupus Corrigens), N. F. VIII.—Potassium Hydroxide Solution (25 cc.) is used with Eriodictyon Fluidextract (32 cc.) and other ingredients to prepare 1000 cc. of the syrup. The active principle, a bitter acrid resin, eriodictyol, is insoluble in neutral or acid aqueous solution. The potassium hydroxide forms soluble compounds with the resin. Magnesium carbonate, used as a clarifying agent, also contributes to the alkalinity of the syrup. It is used for masking the taste of bitter basic compounds such as quinine and strychnine. It is ineffective with acidic substances such as barbital and is incompatible with acids and acid salts. The tannin present makes it unsuited for iron preparations. Average dose—8 cc. (approximately 2 fluidrachms).

8. *Copaiba Mixture* (Mistura Copaibæ, Lafayette Mixture), N. F. VIII.—Copaiba contains a resin composed of about three acids. The potassium hydroxide solution (30 cc.) is used to form water soluble potassium compounds of this resin. The preparation was introduced many years ago for the treatment of gonorrhea and since then has been used for about every ill known to man. Its value as a therapeutic agent is indeed very questionable (see p. 204). Average dose—8 cc. (approximately 2 fluidrachms).

## POTASSIUM HYPOPHOSPHITE

*Potassium Hypophosphite*, N. F. VIII



**Physical Properties.**—Potassium Hypophosphite occurs as white, opaque, hexagonal plates, but on account of its being extremely deliquescent, it is usually found in crystalline masses, or as a white, granular powder. The salt is odorless and has a pungent, saline taste. It has a specific gravity of 2.338 at  $\frac{20}{4}^{\circ}$  C.

One Gm. of the salt is soluble in about 0.6 cc. of water and in about 9 cc. of alcohol, at  $25^{\circ}$  C.; it is somewhat more soluble in boiling water or boiling alcohol.

Potassium hypophosphite melts at  $96^{\circ}$  C.

**Chemical Properties.**—When potassium hypophosphite is heated, phosphine ( $\text{PH}_3$ ) is evolved and the pyrophosphate is left as a residue (1).



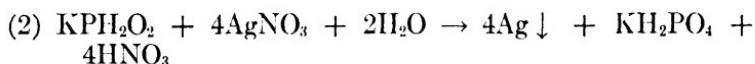
When potassium hypophosphite is heated or triturated with any oxidizing agent (*e. g.*, potassium chlorate, nitrate, or permanganate) it explodes violently. The chemical properties are due to the hypophosphite ion (see Hypophosphorous Acid, p. 115).

**Official Tests for Identity.**—1. An aqueous solution of potassium hypophosphite (1 in 20) is neutral or slightly alkaline to litmus paper.

2. It responds to all tests for potassium (*q. v.*).

3. It responds to all tests for hypophosphites (see Sodium Hypophosphite, p. 195).

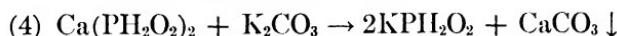
4. An aqueous solution of hypophosphite reacts with silver nitrate to form white silver hypophosphite which is immediately reduced to metallic silver and primary potassium orthophosphate (2).



**Commercial Manufacture.**—1. Potassium hypophosphite may be made by boiling phosphorus with a solution of potassium hydroxide (3). In order to prevent the decomposition of the hypophosphite by any excess alkali, carbon dioxide is passed into the liquid. When the reaction is complete, the solution is carefully evaporated and the potassium hypophosphite dissolved in alcohol, from which it may be granulated or crystallized.



2. The salt is usually made by adding potassium carbonate to a solution of calcium hypophosphite (4).



The precipitated calcium carbonate is filtered off and the filtrate carefully evaporated at reduced pressure and with constant stirring until a granular salt is obtained.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Hypophosphite* (Potassii Hypophosphitis), N. F. VIII.—Potassium Hypophosphite, when dried to constant weight over sulfuric acid, contains not less than 98 per cent of  $\text{KH}_2\text{PO}_2$ .

*Caution should be observed in compounding Potassium Hypophosphate with other substances, as an explosion may occur if it is triturated or heated with nitrates, chlorates, or other oxidizing agents.*

Hypophosphites when administered are excreted almost quantitatively in the urine. They are not oxidized in the tissues to phosphates nor do they contribute to nerve cell metabolism or influence nutrition (see p. 117). Their use as nerve tonics is without foundation. Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains).

2. *Hypophosphites Syrup* (*Syrupus Hypophosphitum*), N. F. VIII.—This syrup contains (per 100 cc.) the hypophosphites of potassium (18 Gm.), calcium (35 Gm.), and sodium (18 Gm.). The syrup is probably of little value (see Sodium Hypophosphate, p. 197). Average dose—8 cc. (approximately 2 fluidrachms).

3. *Compound Hypophosphites Syrup* (*Syrupus Hypophosphitum Compositus*), N. F. VIII.—This syrup contains potassium hypophosphate (1.75 per cent) together with other hypophosphites (Ca, K, Fe, and Mn). The presence of five hypophosphites has no advantage over one in a preparation. Average dose—8 cc. (approximately 2 fluidrachms).

## POTASSIUM IODIDE

### *Potassium Iodide, U. S. P. XIII*

Formula, KI. Molecular Weight, 166.02

**Physical Properties.**—Potassium Iodide occurs as large, transparent and colorless or white and somewhat opaque cubes, or as a white, granular powder. The salt is stable in dry air, but deliquesces slightly in moist air. It has a specific gravity of 3.123 ( $2\frac{1}{4}^{\circ}$  C.) and melts at 773° C., yielding a vapor of normal density. The salt decrepitates when heated.

One Gm. of the salt is soluble in 0.7 cc. of water, in 22 cc. of alcohol, and in 2 cc. of glycerin, at 25° C. One Gm. of it is soluble in 0.5 cc. of boiling water and in 8 cc. of boiling alcohol. When a quantity of potassium iodide is shaken in a test-tube with one-half its weight of water, there is a marked decrease in the temperature of the solution. The phenomenon of solution may be likened to a change in the physical state and hence, the conversion of "solid" potassium iodide into "liquid" potassium iodide through the agency of a solvent would conform to the laws governing such changes, and heat would be absorbed by the molecules of the solute from those of the solvent.

**Chemical Properties.**—Aqueous solutions of potassium iodide take up iodine, forming  $KI_3$ , in equilibrium with dissolved iodine:  $KI_3 \rightleftharpoons KI + I_2$  (in solution). The potassium tri-iodide may be obtained by evaporating the solution over sulfuric acid when black, acicular, monoclinic crystals separate out. These crystals have a specific gravity of 3.498 ( $2\frac{5}{4}^{\circ}$  C.), are very deliquescent, melt at

45° C., and decompose at 100° C. into iodine and potassium iodide. The chemical properties of potassium iodide are due to the iodide ion (see Sodium Iodide, p. 197).

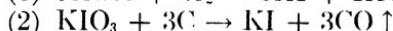
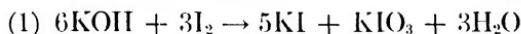
**Official Tests for Identity.**—1. An aqueous solution of potassium iodide is neutral or slightly alkaline to litmus.

2. The salt responds to all the reactions for potassium ion (*q. v.*).

3. A solution of potassium iodide responds to all of the tests for iodide ion (see Sodium Iodide, p. 198).

**Commercial Manufacture.**—Nearly all of the potassium iodide is prepared by adding a slight excess of iodine to a solution of potassium hydroxide to form a mixture of iodide and iodate (see Sodium Iodide, p. 198).

**Laboratory Preparation.**—To the solution of potassium hydroxide obtained in the laboratory preparation of potassium hydroxide (p. 245), or to 100 cc. of a 5 per cent solution of caustic potash, add iodine (about 10 Gm.) until the solution is colored brown (1). The iodine must be added a little at a time in order to avoid any great excess. Evaporate the solution to dryness and powder the residue. Mix about 5 Gm. of powdered wood charcoal with this powder and heat in an iron crucible until slight deflagration takes place (2). Dissolve the potassium iodide in 25 cc. of boiling water, filter, and allow to crystallize. Granulate the salt remaining in the mother liquor after separation of the first crop of crystals.



**Pharmaceutical Preparations and Uses.**—1. *Potassium Iodide* (Potassii Iodidum), U. S. P. XIII.—Potassium Iodide, when dried at 110° for four hours, contains not less than 99 per cent of KI.

The action of potassium iodide is usually characterized by the rather indefinite term "alterative;" however, it does exert a definite influence upon the metabolic processes of the body (see p. 95). Any depressant effect is due to potassium ion. It is used in the treatment of syphilis, chronic articular and muscular rheumatism, goiter, certain forms of asthma and arteriosclerosis (see p. 199). Average dose—0.3 Gm. (approximately 5 grains).

2. *Potassium Iodide Solution* (Liquor Potassii Iodidi, Saturated Potassium Iodide Solution), N. F. VIII.—This solution "contains, in each 100 cc., not less than 97 Gm. and not more than 103 Gm. of KI." The use of heat or hot water is necessary to insure a solution containing the required amount of potassium iodide. When prepared in a pharmacy the correct proportions are 8 drachms (30 Gm.) of potassium iodide and water sufficient to make 1 fluidounce. Since the dose is small and the solution may be used over a period of time the U. S. P. allows the addition of 0.5 Gm. of sodium thiosulfate (per 1000 cc.) which will reduce any liberated free iodine to sodium iodide (see p. 216).

The preparation is used for the effect of the iodide ion (see p. 95). Average dose—0.3 cc. (approximately 5 minims).

3. *Potassium Iodide Tablets* (Tabellæ Potassii Iodidi), N. F. VIII.—These tablets contain not less than 94 per cent and not more than 106 per cent of the labeled amount of potassium iodide for tablets of 0.3 Gm. or more, and not less than 92.5 per cent and not more than 107.5 per cent for tablets of less than 0.3 Gm., including all tolerances. Average dose—0.3 Gm. (approximately 5 grains).

Enteric coated tablets of potassium iodide have recently been introduced because of findings that old solutions of potassium iodide may be unsatisfactory.<sup>1,2</sup>

4. *Iodides Tincture* (Tinctura Iodidorum), N. F. VIII.—(See p. 96.)

5. *Iodine Ointment* (Unguentum Iodi), N. F. VIII.—(See p. 97.)

6. *Phenolated Iodine Solution* (Liquor Iodi Phenolatus), N. F. VIII.—(See p. 98.)

7. *Strong Iodine Tincture* (Tinctura Iodi Fortis), N. F. VIII.—(See p. 98.)

8. *Compound Sodium Salicylate and Gelsemium Elixir* (Elixir Sodium Salicylatis et Gelsemii Compositum), N. F. VIII.—This elixir contains 15 Gm. of potassium iodide in addition to other ingredients in 1000 cc. The potassium iodide is present for the therapeutic effect of the iodide ion. Average dose—4 cc. (approximately 1 fluidrachm).

9. *Potassium Mercuric Iodide* (Potassii Hydrargyri Iodidum), N. N. R.—A complex salt,  $K_2HgI_4$ , formed by the interaction of 1 molecule of mercuric iodide with 2 molecules of potassium iodide. It contains about 25.5 per cent of mercury. It is used as an external germicide much the same as red mercuric iodide and mercuric chloride (see p. 375).

## POTASSIUM NITRATE

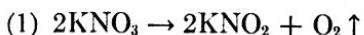
### *Potassium Nitrate*, N. F. VIII

Formula,  $KNO_3$ :  $K-O-N=O$  Molecular Weight, 101.10

**Physical Properties.**—Potassium Nitrate occurs in the form of a white crystalline powder or in long, colorless, transparent six-sided rhombohedrons or prisms. It is odorless, has a saline taste, and produces a cooling sensation in the mouth. It is slightly hygroscopic in moist air. It has a density of 2.11 ( $10.6^\circ C.$ ) and melts without decomposition at about  $337^\circ C.$ .

One Gm. of Potassium Nitrate is soluble in 3 cc. of water, and in about 620 cc. of alcohol at  $25^\circ C.$  One Gm. is soluble in 0.5 cc. of boiling water. It is soluble in glycerin.

**Chemical Properties.**—The salt, when strongly heated, evolves oxygen and is partly reduced to potassium nitrite (1).



<sup>1</sup> New England J. Med., **229**, 670 (1943).

<sup>2</sup> New England J. Med., **229**, 971 (1944).

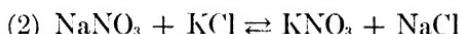
When *crystals* of potassium nitrate are heated, they decrepitate or explosively burst asunder. This is explained by the fact that, even though the salt does not form a hydrate, it occludes a small portion of the mother liquor at the time of crystal formation and the intra-crystal pressure developed by the vaporization of the water causes the more or less violent action. Potassium nitrate also deflagrates when heated with charcoal. The major chemical properties are due to the nitrate ion (see p. 119).

**Official Tests for Identity.**—1. An aqueous solution of potassium nitrate is neutral to litmus paper.

2. Aqueous solutions of the salt respond to all the reactions for *Potassium* ion (see p. 224).

3. The salt gives all the tests for *Nitrate* ion (see p. 120).

**Commercial Manufacture.**—Large quantities of potassium nitrate are made from the comparatively cheap sodium nitrate which occurs naturally in enormous deposits in Chile and Peru. Sodium nitrate and potassium chloride are heated with a small quantity of water when the following reaction takes place (2).



The following observations may be made regarding the solubility of the respective products of the reaction: Except for mutual solubility, about the same quantity of sodium chloride dissolves in a definite volume of water at 0° C. as it does in a like volume of water at 100° C. (35.7 Gm. NaCl in 100 Gm. of water at 0° C., 39.8 Gm. of NaCl in 100 Gm. of water at 100° C.), whereas potassium nitrate is very much less soluble in cold water than it is in hot water (13.3 Gm. of KNO<sub>3</sub> in 100 Gm. of water at 0° C., 247 Gm. of KNO<sub>3</sub> in 100 Gm. of water at 100° C.). Therefore, when the concentrated solution is strained through filter cloth, most of the sodium chloride remains behind, whereas nearly all of the potassium nitrate remains in solution in the hot liquor. When this is allowed to cool, most of the potassium nitrate, on account of its lesser solubility in cold water, crystallizes out, whereas the sodium chloride remains in solution. The solution is constantly stirred during the crystallization of the salt in order to obtain small crystals and to prevent the taking up of water of decrepitation. The crystalline mass is separated from the mother liquor by decantation or by centrifuging and washed with a gentle spray of water in a hydro-extractor or centrifuge machine. The product is dried in copper pans in a current of hot air.

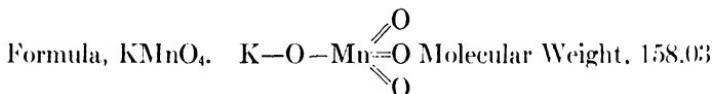
**Laboratory Preparation.**—Dissolve 8.5 Gm. of sodium nitrate and 7.46 Gm. of potassium chloride in 10.5 cc. of distilled water and boil for fifteen minutes, maintaining the original volume of solution by the occasional addition of water. Strain the hot solution through a muslin cloth and cool the filtrate to 10° C. Collect the crystals, wash them with a spray of cold water, and then dry them in a current of hot air.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Nitrate* (*Potassii Nitratas; Saltpeter*), N. F. VIII.—Potassium Nitrate, when dried for four hours at  $10^{\circ}$  C., contains not less than 99 per cent of  $\text{KNO}_3$ . Potassium nitrate is usually employed internally when the action of potassium ion is desired. The nitrate ion is said to increase the rapidity of the absorption of the potassium ion. The nitrate ion produces an irritation of mucous membrane and hence large doses are prohibitive. In medicinal doses potassium nitrate is a diuretic and diaphoretic, although the harmless organic potassium salts are to be preferred. It has the same dangers as other potassium salts when there is faulty kidney elimination.

Stramonium leaves are often burned to volatilize the alkaloidal components to alleviate the paroxysms of asthma. Potassium nitrate is often added to the leaves as an oxidizing agent to facilitate burning. Average dose—1 Gm. (approximately 15 grains).

### POTASSIUM PERMANGANATE

*Potassium Permanganate*, U. S. P. XIII



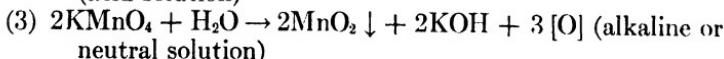
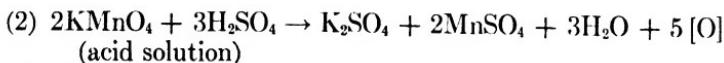
**Physical Properties.**—Potassium Permanganate occurs in the form of odorless, slender, dark purple monoclinic prisms, almost opaque by transmitted light and of a blue metallic luster by reflected light. The color is sometimes modified by a dark bronze-like appearance. It has a specific gravity of 2.703 ( $\frac{20}{4}$ ° C.) and is stable in air. Solutions of potassium permanganate have a sweetish, astringent taste.

One Gm. of the salt is soluble in 15 cc. of water at  $25^{\circ}$  C. and in 3.5 cc. of boiling water. It is reduced by alcohol.

When potassium permanganate is heated it decrepitates, and at about  $240^{\circ}$  C. it decomposes into oxygen, potassium manganate, and manganese dioxide (1).

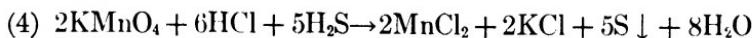


**Chemical Properties.**—This salt is a very powerful oxidizing agent both in the dry state and in solution (2 and 3). Therefore, great care should be exercised in handling it, as dangerous explosions are liable to occur if it comes in contact with organic or other readily oxidizable material, *e. g.*, cork, charcoal, etc., either in solution or in the dry state.



The chemical properties are due to the presence of the permanganate ion which reacts as a strong oxidizing agent toward many easily oxidizable compounds (reducing agents).

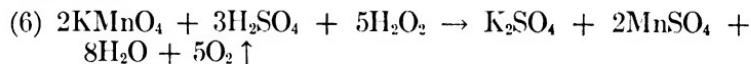
1. When to a solution of potassium permanganate, HCl and H<sub>2</sub>S (reducing agent) are added, it will be noted that the violet color disappears and sulfur (oxidized product) is precipitated. The permanganate ion has been reduced to manganous ion (4).



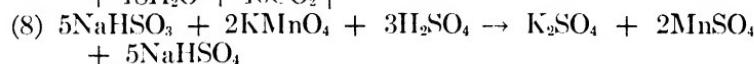
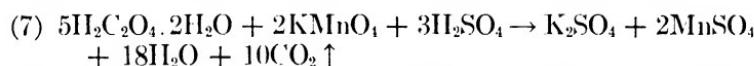
In neutral solution with 1 per cent permanganate the reaction is (5).



2. When a 3 per cent solution of hydrogen peroxide is added to an aqueous solution of potassium permanganate previously acidulated with sulfuric acid, the color of the permanganate solution is discharged (6).



3. An aqueous solution of the salt acidulated with sulfuric acid is decolorized by a solution of oxalic acid in hot solution (7) and by a solution of sodium hydrogen sulfite in cold solution (8).



4. On heating potassium permanganate at 240° C., very pure oxygen is evolved, and a black powdery residue of potassium manganese and manganese dioxide (9) remains.

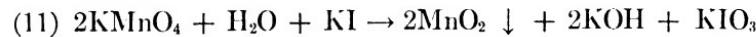


When a little water is added to the residue, a dark green color is formed.

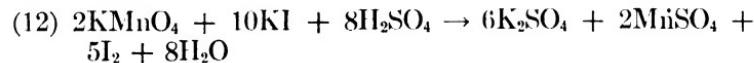
5. Chlorine is produced by the action of hydrochloric acid on potassium permanganate (10).



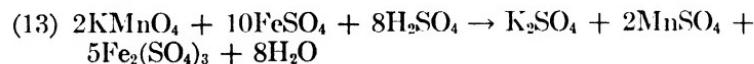
6. Alkaline or neutral solutions of potassium permanganate oxidize iodides to iodates (11).



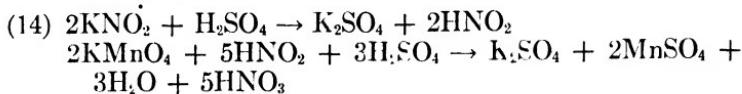
7. Iodine is liberated from potassium iodide by an acid solution of potassium permanganate (12).



8. Ferrous salts are readily oxidized to ferric salts (13) by potassium permanganate in acid solution.



9. Nitrites are oxidized to nitrates by potassium permanganate in acid solution (14).



10. Sulfuric acid is formed when sulfur dioxide is oxidized with permanganate (15).



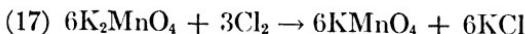
**Official Tests for Identity.**—1. A concentrated aqueous solution of Potassium Permanganate is deep violet red in color. Very dilute solutions are rose colored.

2. Solutions of potassium permanganate acidified with sulfuric acid are decolorized by solutions of hydrogen peroxide (6), by sodium bisulfite T.S. (8) in the cold, and by hot oxalic acid T.S. (7).

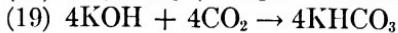
**Commercial Manufacture.**—This salt is prepared by mixing 1000 pounds of a solution of potassium hydroxide (specific gravity, 1.44) with 360 pounds of powdered manganese hydroxide and 210 pounds of potassium chlorate. The mixture is boiled, evaporated and the residue heated in iron pans until it has acquired a pasty consistency (16).



The potassium manganate (green) thus obtained is boiled with a large quantity of water, and at the same time a current of chlorine (17) carbon dioxide (18, 19) or ozonized air is passed into the liquid until the potassium manganate is completely converted to permanganate. The  $\text{MnO}_2$  formed is removed continuously in order to prevent its breaking down the permanganate formed.



or



The solution of potassium permanganate is drawn off from any precipitate of manganese dioxide, concentrated and crystallized. The crystals are then centrifuged and dried.

**Laboratory Preparation.**—Place 10.5 Gm. of potassium hydroxide in a porcelain evaporating dish and add 35 cc. of water. When solution is effected, add 9 Gm. of pyrolusite (87 per cent  $\text{MnO}_2$ ) and 5.25 Gm. of potassium chlorate and, with constant stirring, evaporate the mixture to a thick paste. Transfer the mixture to an iron dish or crucible and heat to redness until water ceases to be driven off. Then allow the greenish-brown mass to cool, remove it from the crucible and powder it. (Caution, see p. 255.) Mix the powder with 125 cc. of water and boil, *slowly* passing carbon dioxide into the boiling liquid until a piece of filter paper immersed in the liquid and then dried gives a purple color only. Permit the precipitate to subside and filter it through asbestos. Wash the precipitate with

a small quantity of water and evaporate the combined filtrates until crystals begin to form. Filter the liquid several times during the evaporation. Separate the crystals from the mother liquor and evaporate the latter in order to obtain a second crop.

The reactions involved in the laboratory method are the same as occur in the manufacture of this salt on a large scale (*q. v.*). In the process it should be noted that the carbon dioxide must be passed into the boiling liquid at such a rate that practically all of it is absorbed. Great care should be taken to prevent any dirt or soot from falling into the permanganate solutions.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Permanganate* (Potassii Permanganas), U. S. P. XIII.—Potassium Permanganate, when dried over sulfuric acid for eighteen hours, contains not less than 99 per cent of  $KMnO_4$ . *Caution.*—*Great care should be observed in handling potassium permanganate, as dangerous explosions are liable to occur if it is brought in contact with organic or other readily oxidizable substances, either in solution or in the dry state.*

Potassium permanganate belongs to the oxidizing class of antiseptics. A solution of the salt when in contact with organic matter, such as albumin or bacteria, at once liberates oxygen. The oxygen oxidizes the protein of the bacteria and kills them. The action of permanganate is of short duration and is limited to the skin and the surface of the mucous membranes. There is very little penetration of this oxidizing action; this makes potassium permanganate of less value than most other antiseptics. A serious drawback to its use is the deposition of brown manganese dioxide over the area to which it is applied.

It is used in the treatment of urethritis and occasionally of gonorrhœa. Solutions varying in strength from 1:500 to 1:15,000 are employed for irrigating the urethra. Due to its oxidizing power it finds some use in Vincent's infection, epidermophytosis, athlete's foot, snake bite, poison ivy and as a chemical antidote in poisoning.

2. *Potassium Permanganate Tablets* (Tabellæ Potassii Permanganatis), N. F. VIII.—These tablets contain not less than 94 per cent and not more than 106 per cent of the labeled amount of potassium permanganate for tablets of 0.3 Gm. or more, and not less than 92.5 per cent and not more than 107.5 per cent for tablets of less than 0.3 Gm., including all tolerances. Average dose—60 mg. (approximately 1 grain).

### POTASSIUM SODIUM TARTRATE

*Potassium Sodium Tartrate*, U. S. P. XIII



Formula,  $\text{KNaC}_4\text{H}_4\text{O}_6 \cdot 4\text{H}_2\text{O}$ ;  $\text{CH}(\text{OII})\text{COONa} \cdot 4\text{H}_2\text{O}$

Molecular Weight, 282.23

In 1672 Pierre Seignette, an apothecary of Rochelle, France, first prepared potassium and sodium tartrate. In allusion to its

discoverer and his native town this compound is called either Rochelle Salt or Sal Seignette.

**Physical Properties.**—Potassium Sodium Tartrate occurs as a white, crystalline powder, or as large, colorless, transparent, rhombic prisms which effloresce slightly in warm, dry air. It is odorless, has a cooling, saline taste, and a specific gravity of 1.783 at  $\frac{20}{4}^{\circ}$ .

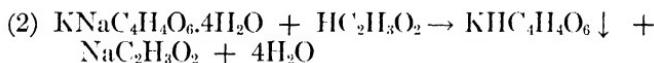
One Gm. of the salt is soluble in 1 cc. of water at  $25^{\circ}\text{ C}$ . It is practically insoluble in alcohol.

Potassium and sodium tartrate melts at about  $74^{\circ}\text{ C}$ . When the temperature is raised, it carbonizes and gives off inflammable vapors having the odor of burnt sugar. Finally, a residue of unburnt carbon and the carbonates of potassium and sodium remains (1).



**Chemical Properties.**—Potassium and sodium tartrate is a salt of strong bases and a weak organic acid. It possesses the characteristics of the alkali salts of organic acids. Aqueous solutions are slightly alkaline due to hydrolysis. It responds to the chemical properties of tartrates discussed on p. 230.

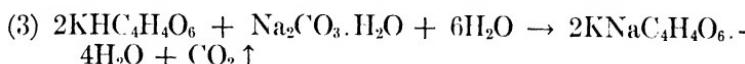
When an equal volume of acetic acid is added to a solution of the salt, a white crystalline precipitate results (2).



**Official Tests for Identity.**—1. A 5 per cent aqueous solution of the salt is alkaline to litmus paper. The color of a 10-cc. portion of the solution is not affected by 1 drop of phenolphthalein T.S. (*q. v.*).

2. The salt gives the flame test for both potassium and sodium (*q. v.*).

**Commercial Manufacture.**—Potassium and sodium tartrate is prepared by neutralizing a solution of sodium carbonate with potassium bitartrate (3). The solution is boiled for a short time and an exact neutrality produced by the addition of either sodium carbonate or potassium bitartrate. The solution is then allowed to stand at  $60^{\circ}\text{ C}$ . for a period of time to permit any calcium tartrate to settle out. It is filtered, concentrated and crystallized.



**Laboratory Preparation.**—Dissolve 3.3 Gm. of monohydrated sodium carbonate in 40 cc. of boiling water and, when solution has been effected, add 10 Gm. of potassium bitartrate and boil for fifteen minutes. Test a few drops of the solution for excess alkali with phenolphthalein and make it exactly neutral by the addition of small quantities of either sodium carbonate or potassium bitartrate. Set the solution aside for a day or two to allow any calcium tartrate (sometimes present as an impurity in cream of tartar) to

settle out. Filter and evaporate to 18 Gm. and allow to crystallize. Do not use heat in drying the crystals as this is an organic compound.

**Pharmaceutical Preparations and Uses.**—1. *Potassium Sodium Tartrate* (Potassii Sodii Tartras, Rochelle Salt), U. S. P. XIII.—Potassium Sodium Tartrate "when rendered anhydrous by drying at 150°, contains not less than 99 per cent of  $KNaC_4H_4O_6$ ." The official salt contains 4 molecules of water of crystallization corresponding to not less than 21 per cent and not more than 26 per cent of water. Depending upon the dose, the action of Rochelle Salt ranges from a mild laxative to an active hydragogue. It is a saline laxative. (See Disodium Phosphate, p. 209.) It has an important use as a constituent in Fehling's solution. (See Copper Sulfate, p. 285.) Average dose—10 Gm. (approximately  $2\frac{1}{2}$  drachms).

2. *Compound Effervescent Powders* (Pulveres Effervescentes Compositi, Seidlitz Powders), U. S. P. XIII.—The mixture in a blue paper weighs not less than 9.5 Gm. and not more than 10.5 Gm. and contains not less than 23 per cent and not more than 27 per cent of  $NaHCO_3$ , and not less than 73 per cent and not more than 78 per cent of  $KNaC_4H_4O_6$ . (See Sodium Bicarbonate, p. 155.)

### SULFURATED POTASH

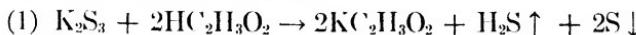
#### *Sulfurated Potash*, N. F. VIII

This substance is not a true chemical compound. It is a mixture composed chiefly of potassium polysulfides and potassium thiosulfate. The N. F. VIII requires that the mixture contain polysulfides equivalent to not less than 12.8 per cent of sulfur.

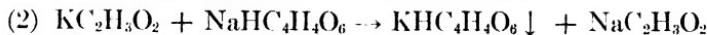
**Physical Properties.**—Sulfurated Potash occurs in irregular pieces having a liver-brown color when freshly made, changing to greenish-yellow and finally to gray through absorption of moisture, oxygen, and carbon dioxide of the air. It has an odor of hydrogen sulfide and a bitter, acrid, alkaline taste.

One Gm. of Sulfurated Potash is soluble in about 2 cc. of water (usually leaving a slight residue), forming a brown solution which is strongly alkaline. Alcohol will dissolve only the sulfides.

**Official Tests for Identity.**—1. When an excess of acetic acid is added to an aqueous solution of Sulfurated Potash, hydrogen sulfide is evolved and sulfur is precipitated (1). The hydrogen sulfide may be recognized by its characteristic odor and by its blackening of moist lead acetate test paper.

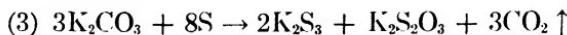


2. If the solution obtained in (1) is filtered and an excess of sodium bitartrate test solution added to the filtrate, an abundant, white, crystalline precipitate will be produced (2).

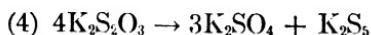


**Commercial and Laboratory Preparation.**—Liver of sulfur is produced commercially by exactly the same process that will be used in its laboratory preparation.

Mix 2 Gm. of sublimed sulfur with 4 Gm. of potassium carbonate and gradually heat them together in a crucible until effervescence ceases (3). Then increase the heat to dull redness or until perfect fusion results. Pour the melt upon a stone slab, covered to prevent access of air, and allow it to cool. Break the solid into pieces and bottle immediately.



When potassium carbonate and sulfur are fused together, a mixture of potassium polysulfides ( $\text{K}_2\text{S}_3$ ,  $\text{K}_2\text{S}_4$ ,  $\text{K}_2\text{S}_5$ ) and potassium thiosulfate is produced and carbon dioxide is evolved. If the temperature of the reaction is not carefully controlled, potassium sulfate may be formed due to the decomposition of the thiosulfate (4).



**Pharmaceutical Preparations and Uses.**—1. *Sulfurated Potash* (Potassa Sulfurata), N. F. VIII.—Synonyms are sulfurated potassa, liver of sulfur, and hepar sulfuris. It is a mixture composed chiefly of potassium polysulfides and potassium thiosulfate. It contains not less than 12.8 per cent of sulfur in combination as sulfide. Sulfurated potash is rarely used internally. Due to the liberation of hydrogen sulfide on contact with the skin, and the alkaline medium which it creates, the compound is used to treat parasitic diseases of the skin. A 10 per cent ointment is used for acne, scabies, ringworm, psoriasis and tinea versicolor.

2. *White Lotion* (Lotio Alba, Lotio Sulfurata), N. F. VIII.—In this lotion sulfurated potash reacts with zinc sulfate to form zinc sulfide. (See Zinc Sulfate, p. 383.)

### POTASSIUM THIOCYANATE

#### *Potassium Thiocyanate*, N. F. VIII

Formula, KSCN. Molecular Weight, 97.17

**Physical Properties.**—Potassium Thiocyanate occurs as colorless, transparent, prismatic crystals that are hygroscopic. It is odorless, and has a cooling, saline taste. It is affected by light. One Gm. of Potassium Thiocyanate is soluble in about 0.5 cc. of water and in about 12 cc. of alcohol, at 25° C.; also in about 0.2 cc. of boiling water and in about 8 cc. of boiling alcohol.

**Chemical Properties.**—The chemical properties are discussed under the sodium salt (see p. 216).

**Official Tests for Identity.**—1. A 10 per cent aqueous solution of the salt is neutral to litmus and responds to all tests for Potassium ion (see p. 223) and for *Thiocyanate* ion (see p. 215).

**Commercial Manufacture.**—The procedure is essentially that for the sodium salt (see p. 215).

**Pharmaceutical Preparations and Uses.**—1. *Potassium Thiocyanate* (Potassii Thiocyanas, Potassium Sulfocyanate, Potassium Rhoda-

nate), N. F. VIII.—Potassium Thiocyanate, when dried to constant weight at 105° C., contains not less than 99 per cent of KSCN. There are two major actions of the thiocyanate ion in the body, namely, an iodide-like effect and a nitrite-like effect. It is the nitrite-like action of relaxing smooth muscle that is desirable for its therapeutic use. In hypertension some relief is obtained because the capillaries are dilated. Also, use of the salt in the treatment of migraine has recently been found of value.<sup>1</sup>

### NON-OFFICIAL POTASSIUM SALTS

**Potassium Sulfate**, K<sub>2</sub>SO<sub>4</sub>, Molecular Weight 174.25.—Potassium Sulfate forms small, hard, colorless, six-sided, rhombic prisms terminated by pyramids. It occurs as a white powder; or as white granules. It is odorless and has a saline, slightly bitter taste. It has a specific gravity of 2.662 (24° C.). The salt is permanent in air.

One Gm. is soluble in 10 cc. of water at 25° C., or in 4 cc. of boiling water. It is insoluble in alcohol.

The salt decrepitates when heated and melts at about 1067° C. At white heat it is partially decomposed.

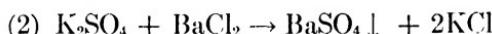
An aqueous solution of potassium sulfate is neutral to litmus paper.

Its solutions respond to all the reactions for potassium ion (*q. v.*).

When an excess of sodium bitartrate test solution is added to a saturated aqueous solution of the salt, a white, crystalline precipitate is produced (1).



A heavy, white precipitate of barium sulfate (insoluble in hydrochloric acid or in other dilute acids) is produced when barium chloride test solution is added to an aqueous solution (1 in 20) of potassium sulfate (2).



Potassium sulfate is sometimes made by treating *sylvite* (almost pure KCl) with sulfuric acid and concentrating the resulting solution to crystallization.

At Stassfurt it is usually prepared by concentrating solutions of *kainite* (K<sub>2</sub>SO<sub>4</sub>.MgSO<sub>4</sub>.MgCl<sub>2</sub>.6H<sub>2</sub>O), when magnesium and potassium sulfates separate out in the form of K<sub>2</sub>SO<sub>4</sub>.MgSO<sub>4</sub>.6H<sub>2</sub>O, called *schönite*. When schönite solutions are concentrated in the presence of an excess of potassium chloride, potassium sulfate and magnesium chloride are produced (3). On account of its lesser solubility (1 to 10 at 25° C.), the former settles out, whereas the latter (MgCl<sub>2</sub>, 1 to 0.6 at 25° C.) remains in solution.



<sup>1</sup> Am. J. Med. Sci., 204, 697, 1942

Concentrated solutions of the mineral *kieserite* ( $MgSO_4 \cdot H_2O$ ) also react with potassium chloride in the same manner.

Large deposits of *polyhalite* ( $2CaSO_4 \cdot MgSO_4 \cdot K_2SO_4 \cdot 2H_2O$ ) have been found in Crane County, Texas. These deposits constitute one of the largest available sources of potash in the United States. The mineral is said to be less soluble than that obtained from the salt beds at Stassfurt in Germany.

Pharmaceutical forms have been Potassium Sulfate, N. F. VI, Artificial Carlsbad Salt, N. F. VI and Effervescent Artificial Carlsbad Salt, N. F. VI.

## CHAPTER XIII

### RUBIDIUM AND CESIUM

#### RUBIDIUM

Symbol, Rb. Valence, 1. Atomic Weight, 85.48; Atomic Number, 37

**History.**—Rubidium was discovered by Bunsen and Kirchhoff in 1861. Employing the spectroscope which he and Kirchhoff had but recently invented, he examined the residue from Durkheim mineral water and found two new, bright lines in the blue portion of the spectrum. He, therefore, named the elements rubidium (red) and cesium (blue) in allusion to their spectra.

**Occurrence.**—Rubidium is widely distributed, but only in small quantities. It occurs, usually along with potassium, in many mineral waters, notably those of Durkheim in Baden. This metal is found in combination in lepidolite, phosphorite, petalite and carnallite. It is found in the ashes of some plants, such as tea, coffee and tobacco.

**Properties.**—Rubidium is a silver-white metal that has a faint yellowish tinge. Its density is 1.53, its melting-point  $38.5^{\circ}\text{ C}.$ , and its boiling-point  $700^{\circ}\text{ C}.$  It should be kept under benzene, petroleum, or other non-oxygen containing liquids. It closely resembles potassium. It inflames spontaneously upon exposure to air and acts energetically when placed in water, decomposing the latter and burning with a violet flame.

Rubidium forms four oxides, having the following compositions:  $\text{Rb}_2\text{O}$ ,  $\text{Rb}_2\text{O}_2$ ,  $\text{Rb}_2\text{O}_3$ ,  $\text{Rb}_2\text{O}_4$ . The formulas of rubidium compounds are analogous to those of corresponding potassium compounds.

**Preparation.**—The discoverer of this element recommended the residues remaining after the preparation of lithium from its minerals, as a source of rubidium. Rubidium chloroplatinate is less soluble than the corresponding potassium salt; therefore, a mixture of their platinum precipitates is repeatedly boiled with small quantities of water, which dissolves the more soluble potassium chloroplatinate. The less soluble rubidium compound is reduced by hydrogen and a chloride is obtained. The hydroxide or carbonate of rubidium may be prepared from the chloride in the usual way, and these, when heated with magnesium powder in a current of hydrogen, yield metallic rubidium.

**Uses.**—Rubidium and its compounds are very seldom used in medicine. If it is used, the action is that of the anion produced by the dissociation of the rubidium salt.

**CESIUM**

Symbol, C's. Valence, 1. Atomic Weight, 132.91;  
Atomic Number, 55

**History.**—Cesium, like rubidium, was discovered by Bunsen. It was the first element discovered by the use of the spectroscope.

**Occurrence.**—Cesium is usually associated with rubidium but in smaller amounts. The largest quantity of the metal occurs in the rare mineral *pollucite* (syn. *pollux*), a cesium-aluminum silicate, found on the Island of Elba and at Hebron, Maine. This mineral is an association of pegmatite minerals and contains 31.4 per cent of cesium oxide. It is found also in the waters of many mineral springs.

**Properties.** Cesium is a silver-white, soft metal, having a density of 1.87 and a melting-point of 28.5° C. It boils at 670° C. Its properties closely resemble those of potassium and rubidium.

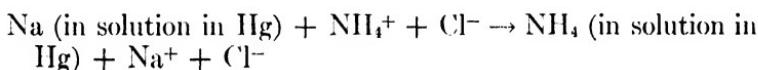
**Preparation.**—Cesium metal is obtained by a process similar to that used for the preparation of rubidium (*q. v.*).

**Uses.**—Cesium and its compounds are of no commercial importance. They are never used in medicine.

## CHAPTER XIV

### AMMONIUM COMPOUNDS

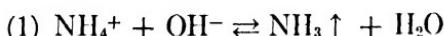
Attention has been called to the fact (p. 74) that when ammonia gas is passed into water, a solution containing dissolved ammonia, undissociated ammonium hydroxide, ammonium ions, and hydroxide ions is produced. The positive ammonium cation behaves in all respects like an alkali metal. It unites with anions to form salts which have a very great physical and chemical resemblance to the corresponding potassium salts with which they are ordinarily isomorphous. When a solution of an ammonium salt is electrolyzed, the ammonium cation, upon its discharge, ordinarily gives ammonia and hydrogen, and thus far, all efforts to isolate the "ammonium metal" have failed. If, however, a mercury cathode is used and an ammonium salt decomposed by electrolysis, the mercury swells to a spongy mass of ammonium amalgam and then gives off the decomposition products of ammonium radical, *viz.*, ammonia and hydrogen. Likewise, if sodium amalgam is added to a strong solution of an ammonium salt ( $\text{NH}_4\text{Cl}$ ), an amalgam having a metallic luster is produced. This physical property of the amalgam points strongly toward the metallic character of the ammonium radical.



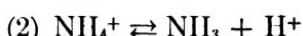
By virtue of the formation of such an amalgam, and because only metals are miscible with mercury, it may be assumed that, if "ammonium" is ever isolated, it will have the physical and chemical properties of a metal.

\***Chemical Properties of the Ammonium Ion.**—Although Ammonia has already been discussed (see p. 70), there are a few general reactions of ammonium compounds which are worthwhile mentioning.

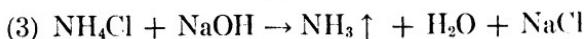
The addition of strong bases, *e. g.*,  $\text{NaOH}$ ,  $\text{KOH}$ , etc., to aqueous solutions of ammonium salts causes the evolution of ammonia when the solution is heated. The reaction is represented as taking place between ammonium ions ( $\text{NH}_4^+$ ) and the introduced hydroxyl ions ( $\text{OH}^-$ ) as follows (1):



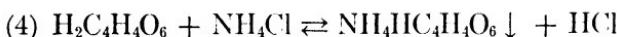
The above reaction illustrates very nicely the Lowry-Brönsted concept of acids and bases, inasmuch as the ammonium ion is essentially an acid which is capable of ionizing into ammonia and a proton (2), and the hydroxyl ion is a strong base capable of combining with the proton (1).



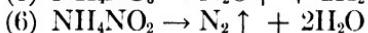
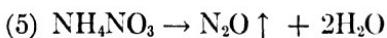
The reaction of ammonium salts with strong bases is made use of in testing for ammonium compounds and also in the preparation of small amounts of ammonia gas for laboratory use, as for example from ammonium chloride (3).



Ammonium salts will form a white, crystalline precipitate of ammonium bitartrate with tartaric acid (4). If this reaction mixture is buffered with a little sodium acetate to remove the protons (as relatively non-ionized acetic acid) the precipitate forms with much more readiness.



Ammonium salts in general are rather unstable and may decompose under conditions varying from room temperature to strong heating. Many of the ammonium salts are volatilized without decomposition on heating, but if any one of them is heated in a closed tube it will decompose. Among the salts which are not volatilized by heating are the borate, phosphate, chromate and vanadate. Practically all of the ammonium salts (*q. v.*) will liberate ammonia on decomposition with the exception of ammonium nitrate (5) and nitrite (6).



**Official Test for Identity of Ammonium Ion.**—The test for ammonium salts is carried out by adding an excess of sodium hydroxide T.S. to the salt (1). A positive test is obtained if ammonia is evolved. The ammonia may be recognized by its odor or by the fact that it turns moistened red litmus paper blue. If the solution is warmed, the decomposition is accelerated because ammonia is less soluble in hot solutions than in cold.

**Pharmacology of the Ammonium Ion.**—The pharmacology of the ammonium ion falls into certain more or less well-defined categories, namely (1) acid-base equilibrium of the body, (2) diuretic effect, and (3) expectorant effect.

1. Ammonium ion plays a rather important rôle in the maintenance of the acid-base equilibrium of the body, particularly in combating acidosis.

It had been known that ammonia was rapidly converted to urea in the body, but it was only after the realization that the kidney was capable of reconverting urea to ammonia that the full importance of ammonia in the body economy was understood. By its ability to excrete ammonia (essentially ammonium ion) the kidney saves base (*e. g.*, sodium) for the body by substituting the ammonium cation for the base cation in the compounds being excreted. The effect of conserving base to prevent acidosis is well known and has been touched upon previously (see p. 152).

2. The diuretic effect of certain ammonium salts has been exhaustively investigated and its mechanism elucidated. Large amounts of salts such as ammonium chloride (or ammonium nitrate) will cause an acidosis due to the conversion of the ammonium ion to urea and the consequent liberation of hydrochloric acid. The hydrochloric acid, of course, does not remain as such but is instantly neutralized by the alkali reserve of the body (mostly bicarbonate), and the subsequent decrease in the alkali reserve is said to represent an acidosis. It is well to remember that when the body is in a condition of acidosis it does not mean that the pH of the blood has changed significantly but that the alkali reserves of the blood have been drawn upon to such a point as to no longer be at normal level. The exact reason as to why the diuretic effect is brought about by the acidosis has not been settled. Whether it is a defense mechanism of the body in which excess salts are removed or whether it is primarily a removal of water with the salts being present only to maintain proper osmotic levels in the blood is not known.

3. The expectorant action of the ammonium salts is probably due to local irritation which in turn is due to a salt action, but this is merely a postulation. However, the ammonium salts have been used extensively in the treatment of coughs associated with a thick viscid sputum. The action of the ammonium salt is to thin out and perhaps increase the quantity of the mucus. Ammonium chloride and ammonium carbonate particularly have been used in cough preparations.

#### OFFICIAL AMMONIUM COMPOUNDS

##### AMMONIUM BROMIDE

###### *Ammonium Bromide*, N. F. VIII

Formula,  $\text{NH}_4\text{Br}$ . Molecular Weight, 97.96

**Physical Properties.**—Ammonium Bromide occurs as colorless, prismatic, cubical crystals, or as a white, crystalline or granular powder. It is odorless and has a pungent, saline taste. It is slightly hygroscopic and, when exposed to the air, it undergoes slight decomposition and acquires a yellowish color. It has a density of about 2.548.

One Gm. of Ammonium Bromide dissolves in about 1.3 cc. of water and in about 12 cc. of alcohol, at  $25^\circ \text{C}$ . One Gm. is soluble in about 0.9 cc. of boiling water and in about 1.2 cc. of boiling alcohol. It is soluble in ether.

When the salt is heated, it volatilizes completely without decomposition.

**Chemical Properties.**—This salt has all of the activity mentioned under Chemical Properties of Ammonium Ion, together with the reactions of the bromide ion (see Sodium Bromide, p. 164).

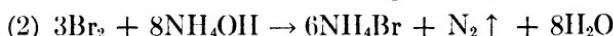
**Official Tests for Identity.**—1. The salt gives the test for *Ammonium* (*q. v.*).

2. The salt gives the tests for *Bromide*. (See p. 140).

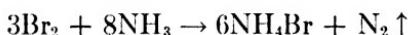
**Commercial Manufacture.**—This salt is prepared by mixing boiling solutions of ammonium sulfate and potassium bromide (1). When the liquid is cooled, most of the potassium sulfate settles out. After the solution has been concentrated to about one-half its volume, it is again allowed to cool and alcohol added to facilitate the precipitation of the remaining potassium sulfate. Then the clear liquid is concentrated to crystallization or evaporated to dryness with constant stirring to form the granular salt.



Although ammonium bromide may also be made by neutralizing hydrobromic acid with ammonium hydroxide, it is customary to utilize the reaction between the cheaper bromine and ammonia (2).



or



When the reaction is completed the solution is evaporated to dryness to obtain the crystalline ammonium bromide.

**Laboratory Preparation.**—Dissolve 23.8 Gm. of potassium bromide in 25 cc. of boiling water and 13.2 Gm. of ammonium sulfate in 15 cc. of boiling water. Mix the boiling solutions and stir well. When the solution has cooled to about 70° C., add 20 cc. of alcohol. Cool the mixture to room temperature, separate the precipitated potassium sulfate by filtration through a pledget of cotton placed in a funnel and wash the residual salt with 35 per cent (by volume) alcohol. Carefully evaporate the filtrate containing the ammonium bromide on a water-bath and allow the salt to crystallize.

**Pharmaceutical Preparations and Uses.**—1. *Ammonium Bromide* (*Ammonii Bromidum*), N. F. VIII.—Ammonium Bromide, when dried over sulfuric acid for twenty-four hours, contains not less than 99 per cent of NH<sub>4</sub>Br. Ammonium bromide is used for the activity of the bromide ion (*q. v.*) which is sedative. In doses large enough to produce the physiological effect of the bromide ion, the salt is irritating to mucous membranes. Therefore, it is best administered in small doses in combination with other bromides, *e. g.*, sodium and potassium bromides. Although the preparations containing mixed bromides are quite popular, there is much question as to whether there is any advantage in administering the mixture as contrasted to a single salt, *e. g.*, sodium bromide. A technical grade of the salt is used in photography, lithographing and in engraving. Average dose—1 Gm. (approximately 15 grains).

2. *Ammonium Bromide Elixir* (*Elixir Ammonii Bromidi*), N. F. VIII.—This elixir contains in each 100 cc., not less than 8 Gm. and not more than 9 Gm. of ammonium bromide, NH<sub>4</sub>Br. It is prepared by dissolving 85 Gm. of ammonium bromide in 460 cc. of distilled water, adding 200 cc. of syrup and bringing the volume up to 1000 cc. with aromatic elixir. It is used as a sedative. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Five Bromides Elixir* (*Elixir Bromidorum Quinque*), N. F. VIII.—This elixir contains 1.7 per cent of ammonium bromide together with varying percentages of other bromides (Na, K, Ca, and Li). It is used for its sedative properties. Average dose—4 cc. (approximately 1 fluidrachm).

4. *Bromides Syrup* (*Syrupus Bromidorum*), N. F. VIII.—This syrup contains 5 per cent of ammonium bromide with varying quantities of other bromides (K, Na, Ca, and Li). It is used as a sedative. Average dose—4 cc. (approximately 1 fluidrachm).

5. *Three Bromides Elixir* (*Elixir Bromidorum Trium*), N. F. VIII.—This elixir contains 8 per cent each of ammonium, potassium and sodium bromides. It is used as a sedative. Average dose—4 cc. (approximately 1 fluidrachm).

6. *Three Bromides Tablets* (*Tabellæ Bromidorum Trium, Triple Bromide Tablets*), N. F. VIII.—These tablets contain the bromides of ammonium, potassium and sodium in equal proportions and show a content of bromine not less than 70 per cent and not more than 81 per cent of the labeled amount of total bromides, including all tolerances. “The tablets show a content of ammonium bromide not less than 30.8 per cent and not more than 35.8 per cent of the labeled amount of total bromides.” They are usually available containing  $2\frac{1}{2}$  grains or 5 grains of each bromide in each tablet. Average dose—0.3 Gm. (approximately 5 grains) each of Ammonium Bromide, Potassium Bromide, and Sodium Bromide.

### AMMONIUM CARBONATE

*Ammonium Carbonate*, U. S. P. XIII

Formula,  $(\text{NH}_4\text{HCO}_3)_n \cdot (\text{NH}_4\text{CO}_2\text{NH}_2)_n$

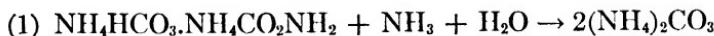
Molecular Weight of  $\text{NH}_4\text{HCO}_3$ , 79.06

Molecular Weight of  $\text{NH}_4\text{CO}_2\text{NH}_2$ , 78.07

**Physical Properties.**—Ammonium Carbonate occurs in the form of white, hard, translucent masses or “cubes,” having a strong odor of ammonia, without empyreuma, and with a sharp, ammoniacal taste. It contains between 30 and 33 per cent of  $\text{NH}_3$ . When exposed to the air, it loses both carbon dioxide and ammonia and is converted into porous, opaque, easily broken lumps or a white powder, the latter consisting chiefly of ammonium bicarbonate,  $(\text{NH}_4\text{HCO}_3)$ .

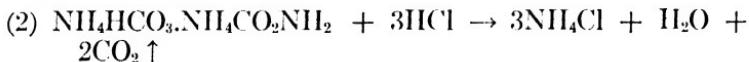
One Gm. of the salt is slowly soluble in about 4 cc. of water at  $25^\circ \text{ C}$ . It is decomposed by hot water into carbon dioxide and ammonia and upon prolonged boiling it is completely decomposed into the aforementioned volatile products.

**Chemical Properties.**—Although this salt actually contains little, if any, normal ammonium carbonate,  $(\text{NH}_4)_2\text{CO}_3$ , it is readily converted into the normal carbonate by dissolving it in dilute ammonia water (1).



The decomposition of the salt from its original hard, translucent state to that of a white powder is caused entirely by loss of ammonia from the ammonium carbamate to give ammonium bicarbonate. Only the hard translucent pieces composed of approximately equivalent parts of ammonium bicarbonate and ammonium carbamate are to be used for prescription compounding.

The salt is decomposed, either dry or in solution by the addition of acids (2). This constitutes one of its principal incompatibilities, although occasionally the combination of acidic ingredients with the salt is intentional.

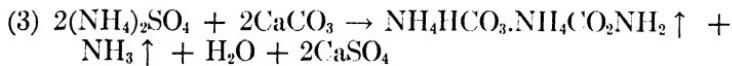


Because of hydrolysis, the aqueous solutions of the salt are alkaline in reaction.

**Official Tests for Identity.**—1. When heated, the salt is volatilized without charring and the vapor is strongly alkaline to moistened litmus paper.

2. A 1 in 20 aqueous solution of the salt effervesces with acids (2).

**Commercial Manufacture.**—1. Large quantities of ammonium carbonate are made by heating ammonium sulfate with an excess of calcium carbonate (chalk) in iron retorts, condensing the vapors of the salt in leaden chambers (3) and recovering the liberated ammonia by passing it into sulfuric acid. The product thus obtained is purified of emphyreuma by sublimation either with or without a small quantity of charcoal. The reaction taking place may be represented in a general way by the following equation:



Occasionally, ammonium chloride (4) is used in place of ammonium sulfate but it is more expensive. Sometimes, barium carbonate is used in place of chalk for the reason that a valuable by-product may be obtained.

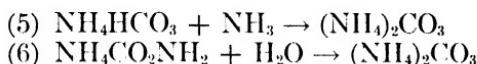


2. Crude commercial ammonium carbonate has been made by introducing ammonia (liberated from ammoniacal gas liquors by lime), carbon dioxide and steam into lead-lined chambers.

**Pharmaceutical Preparations and Uses.**—1. *Ammonium Carbonate* (*Ammonii Carbonas*), U. S. P. XIII.—This salt “consists of ammonium acid carbonate ( $\text{NH}_4\text{HCO}_3$ ) and ammonium carbamate ( $\text{NH}_2\text{COO.NH}_4$ ) in varying proportions, and yields not less than 30 per cent and not more than 33 per cent of  $\text{NH}_3$ .” The salt is also known by the common names: *Ammonium Sesquicarbonate*, *Sal Volatile*, *Preston Salt* and *Hartshorn*. It is widely used for its ability to cause reflex stimulation by inhalation of  $\text{NH}_3$  fumes in conditions of syncope (fainting). The so-called “smelling salts”

used for this purpose usually contain ammonium carbonate together with an ammonia solution. Internally, ammonium carbonate is used for its expectorant properties. A technical grade is used in baking powders, and in a number of industries, *e. g.*, tanning, glue, rubber and dyeing. Average dose—0.3 Gm. (approximately 5 grains).

2. *Aromatic Ammonia Spirit* (*Spiritus Ammoniae Aromaticus*), U. S. P. XIII.—This Spirit contains, in each 100 cc., not less than 1.7 Gm. and not more than 2.1 Gm. of total NH<sub>3</sub>; and ammonium carbonate, corresponding to not less than 3.5 Gm. and not more than 4.5 Gm. as (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub>. Translucent pieces of ammonium carbonate are dissolved by gentle agitation in the diluted ammonia solution previously diluted with distilled water. It is then allowed to stand for twelve hours to effect the conversion of the official ammonium carbonate into normal ammonium carbonate (5 and 6).



The aqueous solution of normal ammonium carbonate is gradually added to an alcoholic solution of the oils of lemon, lavender, and nutmeg, and sufficient distilled water added to make the required volume. After standing in a cool place for twenty-four hours with occasional agitation, the product is filtered in a covered funnel.

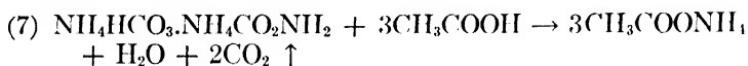
This preparation is a solution of normal ammonium carbonate in an aromatic liquid containing from 62 to 68 per cent of alcohol by volume. Sufficient ammonium hydroxide has been allowed by the formula to completely convert all of the ammonium bicarbonate (present as an integral part of official ammonium carbonate) into normal ammonium carbonate. Therefore, if translucent pieces of official ammonium carbonate have been used, the alcohol-insoluble ammonium bicarbonate will have been converted into normal ammonium carbonate which is completely soluble in 62 to 68 per cent alcohol. Upon exposure to air, official ammonium carbonate loses carbon dioxide and ammonia and is converted into a white, opaque, powdery substance which is chiefly ammonium bicarbonate. If this material, instead of translucent pieces, is employed, there is not sufficient ammonium hydroxide allowed by the formula to convert the large excess of ammonium bicarbonate into normal ammonium carbonate. This fact becomes apparent only when the clear aqueous solution of normal ammonium carbonate and ammonium bicarbonate is poured into the alcoholic solution of the oils, when the ammonium bicarbonate is thrown out of solution as an exceedingly fine precipitate that defies removal by filtration.

Aromatic ammonia spirit is nearly colorless when freshly prepared. On standing, it gradually acquires a yellow color, which is thought to be caused by the action of liberated ammonia upon either the essential oils or the aldehydes present in the alcohol. The color does not impair the medicinal value of the spirit.

When mixed with four or five times its volume of water, it is administered internally as a stimulant, carminative, and antacid.

Its action as a stimulant comes from its ability to stimulate the gastric reflex and not from any direct action on the respiratory or circulatory centers. It is the menstruum used in the preparation of Ammoniated Guaiac Tincture, N. F. VIII. Average dose—2 cc. (approximately 30 minimis).

3. *Ammonium Acetate Solution* (*Liquor Ammonii Acetatis*), N. F. VIII.—This preparation was formerly known as *Spirit of Mindererus*. It is defined as a solution containing in each 100 cc. not less than 6.5 Gm. and not more than 7.5 Gm. of ammonium acetate ( $\text{CH}_3\text{COONH}_4$ ), with small amounts of acetic and carbonic acids. It is prepared by dissolving without strong agitation, 50 Gm. of hard, translucent pieces of ammonium carbonate in enough diluted acetic acid to make 1000 cc. (7).



The N. F. VIII gives an alternate method of preparation. Any desired quantity of a stock solution containing 100 Gm. of ammonium carbonate in sufficient distilled water to make 1000 cc. is mixed with an equal volume of a second stock solution made by diluting 320 cc. of acetic acid with sufficient distilled water to make 1000 cc. Only a freshly prepared solution should be dispensed, because on standing it loses carbon dioxide and becomes less palatable. It is used as a diuretic and diaphoretic. It is also used to prepare Iron and Ammonium Acetate Solution (see p. 620). Average dose—15 cc. (approximately 4 fluidrachms).

4. *Bismuth Magma* (*Magma Bismuthi*, Milk of Bismuth, Cream of Bismuth), N. F. VIII.—Ten Gm. of ammonium carbonate, together with varying quantities of other ingredients are used in preparing 1000 cc. of the finished magma. In making this preparation, the ammonium carbonate is dissolved in an excess of diluted ammonia solution to convert it to normal ammonium carbonate. This normal carbonate reacts with a small amount of the bismuth nitrate, which is added to the ammonia water, to form bismuth carbonate. The bismuth carbonate is unstable in the presence of excess water and hydrolyzes to the form of bismuth subcarbonate. For a more extensive discussion complete with reactions, see p. 548. Average dose—4 cc. (approximately 1 fluidrachm).

5. *Expectorant Mixture* (*Mistura Pectoralis*, Stoke's Expectorant), N. F. VIII.—This preparation contains 1.8 per cent of ammonium carbonate together with several other ingredients. The ammonium carbonate is used in this preparation for its expectorant action. Average dose—4 cc. (approximately 1 fluidrachm).

### AMMONIUM CHLORIDE

*Ammonium Chloride*, U. S. P. XIII

Formula,  $\text{NH}_4\text{Cl}$ . Molecular Weight, 53.50

**Physical Properties.**—Ammonium Chloride occurs in the form of a white, fine or coarse, crystalline powder. Technical grades occur

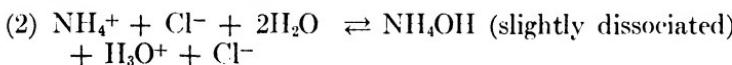
as concave-convex cakes of tough, fibrous crystals. The salt is odorless, has a cooling, salty taste and a density of about 1.536. It is slightly hygroscopic.

Ammonium Chloride is very soluble in water; 1 Gm. dissolving in 2.6 cc. of water, at 25° C. and in 1.4 cc. of boiling water. One Gm. of the salt is soluble in about 100 cc. of alcohol and in about 8 cc. of glycerin, at 25° C.

**Chemical Properties.**— Ammonium chloride is volatilized when heated, but is not decomposed in the process. It is said that the salt decomposes reversibly when heated (1), but the components reunite when cooled again. It is impossible to obtain ammonia from ammonium chloride by ordinary heating.



Freshly prepared solutions of ammonium chloride are neutral in reaction, but, due to hydrolysis (2), the solutions become slightly acid in reaction on standing.



All other reactions of ammonium chloride are typical of ammonium (*q. v.*) or chloride ion (*q. v.*), respectively.

**Official Tests for Identity.**— 1. A 1 in 10 solution responds to the test for *Ammonium* (*q. v.*).

2. The solution also responds to the tests for *Chloride* (*q. v.*).

**Commercial Manufacture.**— Sal ammoniac (crude ammonium chloride) was first prepared by the Egyptians by subliming the ashes resulting from the slow burning of camels' dung. It also has been made by the direct union of equal volumes of ammonia and hydrogen chloride in the presence of a small amount of moisture.

Ammonium chloride is prepared today by a process analogous to that used for making ammonium sulfate. Ammoniacal gas liquors are treated with lime and the liberated ammonia passed into hydrochloric acid. The salt is purified by crystallization and sublimation. The latter operation is carried on in cast-iron pots lined with fire clay and having a dome of glass or earthenware. The charge is first mixed with about 5 per cent of calcium phosphate in order to prevent any volatile iron salts from subliming and then packed tightly in the pot. The lid is clamped on and heat gently applied to drive off any hygroscopic water through a small hole in the cover. The heating is continued until the sublimate is from 5 to 12 cm. thick. Then the cover is lifted and the cake removed. Oftentimes, large cakes of sal ammoniac will be concave-convex, due to the shape of the condenser dome. Crystalline and granular ammonium chlorides are prepared by adding a hot, concentrated solution of the salt to powdered ammonium chloride. The crystalline magma that results is drained, pressed, and dried in moulds.

**Pharmaceutical Preparations and Uses.**— 1. *Ammonium Chloride* (*Ammonii Chloridum, Muriate of Ammonia*), U. S. P. XIII.— Ammonium Chloride, when dried over sulfuric acid for four hours,

contains not less than 99.5 per cent of  $\text{NH}_4\text{Cl}$ . This salt is also known as *Sal Ammoniac*. Because of the characteristic action of the ammonium ion in thinning the secretions, particularly the saliva and mucus, this salt is a valuable expectorant. It probably increases the amount of mucus and at the same time makes it less viscous and tenacious. Large doses act as a diuretic. This action has been discussed previously under the Pharmacology of the Ammonium Ion. Average dose—Expectorant, single dose, 300 mg. (approximately 5 grains). Diuretic, daily dose, 4 Gm. (approximately 60 grains).

2. *Ammonium Chloride Capsules* (*Capsulæ Ammonii Chloridi*), U. S. P. XIII.—These capsules “contain not less than 93 per cent and not more than 107 per cent of the labeled amount of  $\text{NH}_4\text{Cl}$ .” The capsules are used for the purposes given above. The usual capsules available contain 5 and  $7\frac{1}{2}$  grains of  $\text{NH}_4\text{Cl}$ , respectively. Average dosage of Ammonium Chloride—Diuretic, 4 Gm. (approximately 60 grains).

3. *Ammonium Chloride Tablets* (*Tabellæ Ammonii Chloridi*), N. F. VIII.—These tablets “contain not less than 94 per cent and not more than 106 per cent of the labeled amount of  $\text{NH}_4\text{Cl}$  for tablets of 0.3 Gm. or more, and not less than 92.5 per cent and not more than 107.5 per cent for tablets of less than 0.3 Gm.” Both 5-grain and  $7\frac{1}{2}$ -grain tablets of ammonium chloride are available. In addition to the ordinary uncoated tablet described here it is possible to obtain enteric coated tablets which are said to be less irritating to the gastric system. The very fact that enteric coated tablets are less irritating to the gastric system lessens its expectorant effect, although it does not minimize its diuretic potency. Therefore, to obtain the expectorant action it would be advisable to avoid the use of enteric coated tablets. Average dose—0.3 Gm. (approximately 5 grains) of Ammonium Chloride.

## AMMONIUM IODIDE

### *Ammonium Iodide*, N. F. VIII

Formula,  $\text{NHLI}$ . Molecular Weight, 144.96

**Physical Properties.**—Ammonium Iodide occurs as small, colorless, cubical crystals, or as a white, granular powder. It is odorless, has a sharp, saline taste, and a density of 2.56. The salt absorbs moisture very readily. Upon exposure to air and light, it loses ammonia and soon becomes colored yellow or yellowish-brown, due to liberated iodine. If the salt is mixed with a small amount of ammonium hypophosphite, the decomposition is markedly retarded or entirely prevented. In fact, the N. F. permits 1 per cent ammonium hypophosphite in the official salt for this purpose.

One Gm. of ammonium iodide is soluble in about 0.6 cc. of water, in about 3.7 cc. of alcohol, and in about 1.5 cc. of glycerin

at 25° C. It dissolves in about one-half its weight of boiling water.

In absence of air, the salt may be sublimed unchanged. However, when it is strongly heated in air, it volatilizes with slight decomposition.

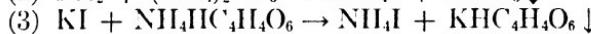
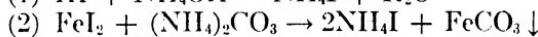
**Chemical Properties.**—An aqueous solution of ammonium iodide is neutral or slightly acid to litmus. In common with many soluble iodides, solutions of ammonium iodide are slowly colored brown upon exposure to air.

In general, the properties of ammonium iodide are a composite of those which may be attributed to the iodide ion (see Sodium Iodide, p. 197) and the ammonium ion (*q. v.*).

**Official Tests for Identity.**—1. The salt in aqueous solution (1 in 20) responds to the test for *Ammonium* (*q. v.*).

2. It also responds to tests for *Iodide* (*q. v.*).

**Commercial Manufacture.**—A number of processes, *e. g.*, neutralization of hydriodic acid with ammonium hydroxide or ammonium carbonate (1), the decomposition of ferrous iodide with ammonium carbonate (2), the interaction of potassium iodide and ammonium bitartrate (3), etc., have been recommended for making ammonium iodide. The method in general use is described under "Laboratory Preparation," and depends upon the reaction between potassium iodide and ammonium sulfate.



**Laboratory Preparation.**—Mix 12.5 Gm. of coarsely powdered potassium iodide and 10 Gm. of ammonium sulfate. Add 10 cc. of boiling water, stir well, and allow the solution to cool slowly. Then add 5 cc. of alcohol, immerse the mixture in a bath of iced water, and stir frequently. Throw the mixture into a glass funnel stoppered with moistened cotton and collect the clear filtrate. Thoroughly wash the crystalline precipitate with diluted alcohol. With constant stirring, evaporate the liquid to dryness. All contact with metals must be avoided. If the finished product contains more than a small amount of potassium sulfate, dissolve it in alcohol, filter from the insoluble potassium sulfate, and evaporate the filtrate as previously described.

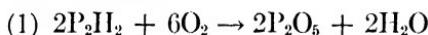
**Pharmaceutical Preparations and Uses.**—1. *Ammonium Iodide* (Ammonii Iodidum), N. F. VIII.—Ammonium Iodide, when dried at 110° for six hours, contains not less than 98 per cent of NH<sub>4</sub>I. It may contain not more than 1 per cent of ammonium hypophosphate as a stabilizing agent. Ammonium iodide is used in all conditions for which iodides are indicated. The presence of the ammonium ion lessens the tendency to depress the circulation, but increases the irritating effect upon the mucous membrane. It is used in the treatment of gout, rheumatism, scrofulosis, etc. Commercially, it is used in photography. Average dose—0.3 Gm. (approximately 5 grains).

## NON-OFFICIAL AMMONIUM COMPOUNDS

1. **Ammonium Hypophosphite** (Ammonii Hypophosphis, N. F. VII),  $\text{NH}_4\text{PH}_2\text{O}_2$ , Molecular Weight, 83.04.—This salt occurs as colorless, odorless, hexagonal plates, or as a granular powder, having a saline and bitter taste. It is very deliquescent.

One Gm. of ammonium hypophosphite is soluble in about 1 cc. of water and in about 20 cc. of alcohol at  $25^\circ \text{ C}$ . It is very soluble in boiling water or boiling alcohol. Solutions are neutral or slightly acid in reaction.

When ammonium hypophosphite is heated, it decomposes into phosphine ( $\text{PH}_3$ , poisonous) and spontaneously inflammable dihydrogen phosphide (1).



In common with other hypophosphites, care should be exercised in triturating or heating the salt with oxidizing agents, *e. g.*, potassium chlorate (2) since explosions are very likely to occur.



Ammonium hypophosphite is usually made by neutralizing diluted hypophosphorous acid with ammonia water (3). During the concentration of the resultant solution, the solution is kept slightly alkaline by the occasional addition of ammonia water. The salt is allowed to crystallize from the concentrated solution or it is carefully granulated.

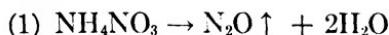


This salt has been deleted from the present N. F. VIII because of the growing conviction among medical practitioners that hypophosphites are of little value in the treatment of conditions for which they have been recommended (see p. 117). Its dose in N. F. VII was 0.2 Gm. (approximately 3 grains).

2. **Ammonium Nitrate**,  $\text{NH}_4\text{NO}_3$ , Molecular Weight, 80.05.—This compound occurs as colorless, odorless, transparent, hygroscopic, deliquescent crystals or white granules with a specific gravity of 1.73. It melts at about  $155^\circ \text{ C}$ . and decomposes at about  $210^\circ \text{ C}$ . into nitrous oxide and water as indicated under "Chemical Properties of the Ammonium Ion," p. 263.

One Gm. dissolves in 0.5 cc. of water at  $25^\circ \text{ C}$ . in 0.1 cc. of boiling water, and in 20 cc. of alcohol. The aqueous solutions have a pH of about 4.

This salt embodies the activities of both the ammonium ion and the nitrate ion, both of which have been discussed previously. However, the fact that nitrous oxide is evolved whenever it is gently heated (1) makes this salt a convenient laboratory source of the gas.

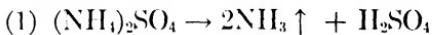


It is made by the action of ammonia upon the dilute acid.

Aside from its technical uses in the manufacture of nitrous oxide (laughing gas), as a fertilizer, in matches as an oxidizing agent, etc., the compound has found a use in medicine as a diuretic. Its mode of action is quite similar to that of ammonium chloride in that the ammonium ion is removed from the body as urea and the nitric acid reduces the alkali reserve. Keith and coworkers<sup>1</sup> state that ammonium nitrate is the most effective of the so-called acid-forming diuretics. The salt is available in 7½-grain enteric coated tablets. A daily dose of 12 Gm. is necessary to produce an effective diuretic action.

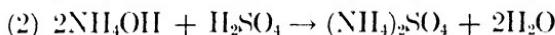
3. **Ammonium Sulfate**,  $(\text{NH}_4)_2\text{SO}_4$ , Molecular Weight, 132.14.— This salt occurs as colorless, odorless crystals or white granules. They have a specific gravity of 1.77. One Gm. of the salt is soluble in 1.3 cc. of cold and in 1 cc. of boiling water. It is insoluble in alcohol. The aqueous solutions have a pH of approximately 5.

This salt decomposes (1) when heated above 280° C.



It forms a double salt with aluminum sulfate quite readily to form the well known *Ammonium Alum* (see p. 442). Its reactions may readily be predicted from a knowledge of the reactions of ammonium (*q. v.*) and sulfate (*q. v.*).

Ammonium Sulfate is manufactured chiefly by passing ammonia-laden gas liquors into dilute sulfuric acid (2). The product is obtained by crystallization and may be purified by recrystallization.



For a pure grade of ammonium sulfate it is desirable to utilize ammonia obtained from other sources than coke-ovens, etc.

Much of the technical grade of ammonium sulfate is used as a fertilizer. The preparation is little used in medicine although a preparation named Ammozyl is used as a local anesthetic. This preparation consists of an aqueous, injectable solution of ammonium sulfate. Its activity is as a regional anesthetic and nerve block for relief of parietal (relating to the wall of any cavity) pain.

4. **Ammonium Thiocyanate** (Ammonium Sulfocyanate or Rhodamide),  $\text{NH}_4\text{SCN}$ , Molecular Weight, 76.11.— This salt occurs as colorless, deliquescent crystals that are easily soluble in water and alcohol.

It is used as a reagent for and in the quantitative determination of As, Sb, Hg, Cu, Ag, and the halogens. In the industries it is employed in the manufacture of matches, explosives, in photography, for strengthening loaded fabrics, etc. Recently this salt has been used as a weed eradicator. When 5 pounds are used per square rod the soil is rendered sterile for about 3 months, after which time fertilizing action is evidenced. The decomposition of iron thiocyanate, formed between the ammonium salts and the iron present in the soil, into fertilizing nitrates is no doubt accomplished by soil bacteria.

<sup>1</sup> Keith, Whelan, and Faunick: Arch. Int. Med., 46, 797 (1930).

## THE COINAGE METALS

### COPPER, SILVER AND GOLD

**Introduction.**—The three members of this family are designated as the “coinage metals” because, from early times, they have been employed for ornamental and for coinage purposes. These elements form Division B of Group I in Mendeléeff’s Table, but their properties differ in many respects from those of the alkali metals which comprise Division A of this same group. It is quite evident that Mendeléeff was cognizant of these facts because he gave them an alternate place in Group VIII. This latter classification associated them with nickel, palladium and platinum to which they are closely related. The differences between the alkali metals and the coinage metals are tabulated below:

#### *Alkali Metals*

- A. Do not occur free in Nature.
- B. Very active chemically; displacing all other elements from their compounds. The chemical activity increases as the atomic weight increases.
- C. Oxides and hydroxides are strongly basic.
- D. Alkali halides are soluble in water, and are not hydrolyzed.
- E. Univalent; forming but one series of compounds.
- F. They form simple cations, never occur in complex anions and do not form complex cations with ammonia.
- G. All are rapidly oxidized in air.

#### *Copper, Silver, Gold*

- A. Occur free in Nature and are easily recovered from their compounds by reduction.
- B. Are low in the electromotive series and hence are not very active chemically; they are displaced by most other metals. The chemical activity decreases as the atomic weight increases.
- C. Oxides and hydroxides are feebly basic (excepting  $\text{Ag}_2\text{O}$  which is an active basic oxide).
- D. Silver, Copper<sup>I</sup> and Gold<sup>I</sup> halides are nearly insoluble in water. With the exception of the silver halides they are readily hydrolyzed and form numerous basic salts.
- E. Copper<sup>I</sup> and Copper<sup>II</sup> each form a series of compounds; Silver,<sup>I</sup> one series; and Gold<sup>I</sup> and Gold<sup>III</sup>, one series each.
- F. All of them form complex ions, e. g.,  $\text{Cu}(\text{CN})_2^-$ ,  $\text{Ag}(\text{CN})_2^-$ ,  $\text{Au}(\text{CN})_2^-$ , copper and silver form complex cations with ammonia, e. g.,  $\text{Ag}(\text{NH}_3)_2^+$ ,  $\text{Cu}(\text{NH}_3)_4^{++}$ .
- G. Copper only is slowly oxidized in air, but rapidly when finely divided and heated in oxygen.

## CHAPTER XV

### COPPER AND COPPER COMPOUNDS

#### **COPPER**

##### *Cuprum*

Symbol, Cu. Valence, I, II. Atomic Weight, 63.54;  
Atomic Number, 29

**History and Occurrence.**—Copper was probably the first metal used by man in fashioning various domestic implements and weapons. Because the metal occurs as such in Nature, the mining and methods of refining it were very simple. The Romans obtained copper from the island of Cyprus and called it *cuprum*, from which the name, *copper*, is derived.

Both free and combined copper occur in Nature. Large deposits of free copper are found in the state of Michigan and in the so-called Lake Superior region. The most important minerals containing combined copper are *chalcopyrite* [CuFeS<sub>2</sub>] and *chalcocite* [Cu<sub>2</sub>S]. These minerals are found in Montana, Utah, Arizona, and in southwest England, Spain and Germany. *Malachite*, a basic copper carbonate [CuCO<sub>3</sub>.Cu(OH)<sub>2</sub>], is found in Siberia, Arizona, the Urals and elsewhere. *Cuprite* or red copper ore [Cu<sub>2</sub>O] occurs abundantly and is one of the most important copper ores. The feathers of certain birds contain pigments in which copper is found.

**Physical Properties.**—Copper is a malleable and ductile metal having a red color by reflected light and a greenish color by transmitted light. Electrolytic copper has a density of 8.92. It melts at 1083° C. and boils at 2310° C. Copper, crystallized in octahedrons, is found in Nature.

Copper is an excellent conductor of heat (surpassed only by silver and gold) and electricity (surpassed by silver), although the presence of small amounts of impurities, especially arsenic, adversely affects the conductivity.

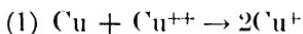
**Chemical Properties.**—The chemical properties of copper and its salts may be conveniently discussed under the headings: (1) copper, (2) cuprous salts and (3) cupric salts.

1. Copper is permanent in dry air, but on exposure to moist air it slowly becomes covered with a green basic sulfate, CuSO<sub>4</sub>.3Cu(OH)<sub>2</sub> (in inland areas) or CuCl<sub>2</sub>.3Cu(OH)<sub>2</sub> (by the sea). This green color was formerly (erroneously) thought to be a basic copper carbonate.<sup>1</sup>

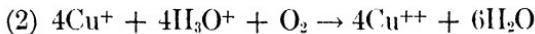
Copper reacts quite readily with oxygen to form cupric oxide (CuO), although when a sheet of copper is heated in air it forms

<sup>1</sup> Mellor's Modern Inorganic Chemistry, revised ed., New York, Longmans, Green & Co., p. 585 (1939)

a thin coating of the black oxide which serves to retard further oxidation. Sulfur and the halogens react more readily with copper than does oxygen. The metal does not react with water nor does it liberate hydrogen from acids since it is below hydrogen in the electromotive series. The only acids which will react with the metal are those which have oxidizing properties, *e. g.*, nitric acid (see p. 119), hot concentrated sulfuric acid (see p. 286), etc. However, metallic copper is dissolved when in contact with an acidified solution of a cupric salt regardless of the acid used. The mechanism whereby this takes place is that the cupric ion (easily reducible) will obtain an electron from the metallic copper atom and in so doing is itself reduced to the cuprous form as well as oxidizing the copper atom to the cuprous form (1).



Then in the presence of atmospheric oxygen and hydronium ions (contributed by the acid) the cuprous ions are oxidized to the cupric form (2).



It has been stated that when copper is heated in air it forms a copper oxide known as cupric oxide. This is not the only oxide of copper, because at least one other common oxide, cuprous oxide ( $\text{Cu}_2\text{O}$ ) exists.

The two copper oxides represent the two forms of oxidation in which copper compounds may exist, namely (1) cuprous ( $\text{Cu}^+$ ) and (2) cupric ( $\text{Cu}^{++}$ ).

2. Although numerous compounds are known in which the copper apparently has a single valence, all of these compounds are water-insoluble and it is questionable whether it is possible to have the cuprous ion in solution in significant concentrations. The cuprous salts, *e. g.*, cuprous chloride, will dissolve in concentrated hydrohalide acids but their state of existence in such a solution is probably not represented by the simple formula,  $\text{CuX}$ , but by a more complex formula of the general type,  $\text{H}_4(\text{Cu}_2\text{X}_6)$ , in which X may be Cl, Br, or I. It is interesting to note that the hydrochloric acid solution of cuprous chloride has an application in gas analysis because of its capacity to absorb carbon monoxide. The reaction is undoubtedly more complex than the following equation indicates (3) but for all practical purposes it may suffice to show what happens.

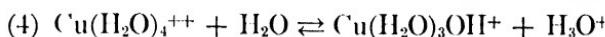


All of the cuprous compounds are white when freshly prepared with the exception of the sulfide ( $\text{Cu}_2\text{S}$ ) which is black and the oxide which is red.

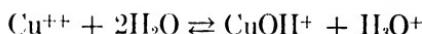
3. Most of the cupric salts are blue in color, some are greenish-blue, and a few have miscellaneous colors. When the water of

crystallization is removed from the salts they usually become white or yellowish in color. The water-soluble cupric salts are the nitrate, chloride, bromide, fluoride, sulfate and acetate. Most of the water-insoluble salts are soluble in acidified solutions. The blue color of aqueous solutions of cupric salts may be attributed to the presence of the blue cupric ion ( $Cu^{++}$ ). Solutions of some cupric salts exhibit a green or brown color but these colors may be ascribed to the presence of undissociated molecules since the solutions will turn blue on dilution.

The cupric ion actually exists in solution in a hydrated form, *i. e.*, it has 4 moles of water,  $Cu(H_2O)_4^{++}$ . This method of representing the ion is not common. The cupric ion has a tendency to hydrolyze (4) and therefore solutions of the salts are usually slightly acidic.

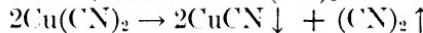
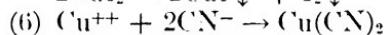
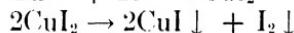
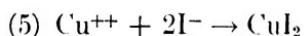


or



It is interesting to note that in this case we have a cation which is subject to hydrolysis. Usually anions are the ones affected.

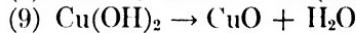
Cupric salts are readily converted to cuprous compounds in many cases, although the anion of the cuprous compound is not necessarily the anion associated with the cupric compound. Falling into this type of reaction we have that of cupric salts reacting with iodides to form cuprous iodide (cupric iodide is quite unstable) and iodine (5) and with cyanides to form cuprous cyanide (6).



An excess of cyanide will redissolve the cuprous cyanide to form the soluble cuprocyanide ion (7).



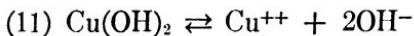
Addition of alkali hydroxides, *e. g.*,  $NaOH$  or  $KOH$ , to solutions of cupric salts results in the precipitation of a light-blue cupric hydroxide (8) which on boiling is converted to brownish-black cupric oxide (9).



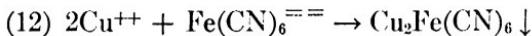
When ammonia water is added to a solution of a cupric salt, a bluish precipitate of cupric hydroxide is formed. However, upon addition of an excess of ammonia water the precipitate redissolves and forms a deep-blue colored solution. The deep-blue color is occasioned by the formation of the cupric-ammonium complexion which is water-soluble and is colored deep blue (10).



The cupric hydroxide precipitate dissolves because the cupric-ammonium complex removes cupric ions from the solution, thus disturbing the equilibrium between the slightly ionized cupric hydroxide and its constituent ions (11), and the cupric hydroxide keeps dissolving in an effort to supply the demand for cupric ions.



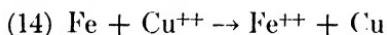
The addition of potassium ferrocyanide to neutral or acidic solutions of cupric salts results in the precipitation of reddish-brown cupric ferrocyanide (12). This precipitate is not soluble in dilute acids but it is quite soluble in excess ammonia water giving the characteristic blue color of the cupric-ammonium complex.



Potassium thiocyanate when added to cupric salts causes the precipitation of insoluble, black cupric thiocyanate (13). This precipitate will gradually turn white upon standing because of formation of white cuprous thiocyanate ( $\text{CuCNS}$ ).



The position of copper in the electromotive series is responsible for its ability to "plate-out" on metallic iron. This is done by placing the iron in a solution of the cupric salt. Since iron is higher in the electromotive series than is copper, the copper is displaced from solution by the iron which becomes ionized (14).



**Official Tests for Copper Ion.**—1. When a bright untarnished surface of metallic iron is introduced into an acidified ( $\text{HCl}$ ) solution of a cupric salt, a red film of copper is deposited on the iron (14).

2. An excess of ammonia T.S. will first produce a bluish colored precipitate of cupric hydroxide (8) which dissolves on addition of more ammonia water to form a deep-blue colored solution (10).

3. Solutions of cupric salts will yield a red precipitate of cupric ferrocyanide when treated with potassium ferrocyanide T.S. (12). The precipitate is insoluble in diluted acids.

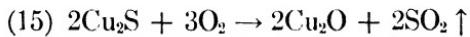
**Commercial Manufacture.**—Most of the metallic copper is obtained from ores containing under 6 per cent copper and it is not infrequent that the ores run less than 1 per cent copper. These ores are mostly sulfide and oxide ores, although a small amount of metallic copper is secured, especially in the Michigan district.

These ores are first crushed to a size to liberate the mineral, which is ordinarily finer than 60 mesh. The flotation process of concentration is used in most cases. The finely crushed ore is mixed with water and a small amount (usually under 1 per cent) of various kinds of oils and soaps. Considerable quantities of other chemical compounds, *e. g.*, lime and acids, are sometimes added to certain ores to meet particular requirements. This mixture is agi-

tated by compressed air or otherwise. This causes small air bubbles to adhere to the mineral particles, and brings them to the surface as a froth or foam which is continuously removed. The process is very efficient and, when properly controlled by adding other chemicals and flotation agents between the various flotation cells, several different froths can be made, each of which will contain a different mineral concentrate. Thus, in complex ores, it is often possible by selective flotation to separate three or four different minerals.

The sulfide concentrate is roasted for the removal of sulfur to the desired point, so that the mixture of ores which is later added to the furnace will contain the proper amount of sulfur (15 and 16). All of the ore, especially oxide ore, is not always roasted, but is often added directly to the furnace. The furnace used is ordinarily the reverberatory type, being approximately 20 to 30 feet wide and 75 to 150 feet long. The fine ore is fed in continuously along the side walls, forming piles reaching almost to the roof, which is usually about 8 feet high. Oil or gas is burned in the furnace to raise the temperature to the melting-point. The furnace is chiefly a melting furnace, although some sulfur is burned off. When the ore is melted, the matte, composed chiefly of copper sulfide of about 40 per cent copper, settles out of the slag which is composed largely of iron oxide and silica, and is tapped off in ladles. This matte in a molten state is poured into a converter which is similar to the Bessemer converter. Air is blown up through the matte, oxidizing the sulfur and the iron present; the latter forming a siliceous slag which is poured off.

The copper thus obtained is usually covered with black blisters, formed by the escape of sulfur dioxide during solidification, and is known as "*blister copper*." It is from 96 to 98 per cent metal but contains some cuprous oxide in solution. It is very brittle. The complete "de-oxidation" of the metal is accomplished by melting the "*blister copper*" and stirring the melted mass with an oak or birch pole. This phase of the refining process is known as "poling." The copper is cast into large plates and then is ready to be purified by electrolysis.



The presence in copper of very small quantities of such impurities as cuprous oxide and sulfide, arsenic, antimony, lead, zinc, gold, silver, etc., materially affects its physical constants and, because its many uses require it to be in a high state of purity, it is usually refined electrolytically. Large, lead-lined tanks are filled with a solution of copper sulfate acidulated with sulfuric acid. Thin sheets of pure copper form the cathodes and "poled-copper" or "blister copper" cast into thick plates serve as the anodes. These are alternately suspended in the electrolyte. A small difference in potential (less than 0.5 volt) is established. This causes the discharge of copper ions ( $\text{Cu}^{++}$ ) with the deposition of metallic copper

on the cathode. On the other hand, the sulfate ions migrate to the anode, where equivalent amounts of copper from the thick plate become ionized. Thus, the concentration of copper ions in the electrolyte remains constant. The anodes are replaced as they are "eaten" away and the cathodes are stripped of the copper deposit, which is about 99.8 per cent pure. The less active metals, *e. g.*, arsenic, antimony, silver and gold, present as impurities in the copper are not ionized because there is a sufficient number of the more active copper ions to carry the current. These metals fall to the bottom of the tank as "electrolytic mud," which is worked for its gold and silver content; the value of the gold and silver often is sufficient to pay for the electrolysis. On the other hand, metals more active than copper, such as zinc, nickel, iron, etc., are readily ionized, but their ions are not discharged at the cathode as long as the more readily discharged copper ions are present.

**Pharmacological Action of the Copper Ion.**—Copper ion is a protein precipitant and, therefore, is an astringent when applied to mucous membranes and abraded surfaces. It is an effective fungicide in minute amounts (1:1,000,000) and has proven of value in the treatment of water to remove algae as well as in fungus infections afflicting humans, *e. g.*, athlete's foot. In spite of its efficiency as a fungicide the copper ion is not an effective bactericide, being only a mild anti-septic in certain selected cases.

Internally, the copper salts have two effects depending upon the dosage in which they are administered: (1) aiding the assimilation of iron and (2) producing emesis.

1. In 1928 Hart, Steenbock and others<sup>1</sup> showed that in animals, iron salts were not well assimilated unless a small amount of a copper salt was present to "catalyze" the assimilation. It was shown shortly thereafter that the same was true in humans. Since that time the use of copper salts along with iron salts in the treatment of the so-called secondary anemias has been more or less accepted. Ordinarily, sufficient copper is obtained in a normal diet to adequately supply the needs of the body. The optimum ratio of copper to iron for maximum utilization of iron is 1:25. In spite of the fact that in many cases it is possible to obtain satisfactory hemoglobin responses with iron salts alone, it is reasonable to believe that copper probably does play an important part in hemoglobin formation.

2. Because of their irritant action, copper salts are prompt acting emetics. The nausea accompanying the emesis is of short duration. Ordinarily, in small doses, the use to produce emesis is safe, but large doses have a corrosive effect on the gastric mucosa and produce characteristic lesions of the kidneys, spleen, and other organs. After its absorption copper is found principally in the form of cupric nucleinate in the liver, blood and bile.

**Uses of Metallic Copper.**—Enormous quantities of copper are used for making motors and dynamos, wire, ornamental vessels, roofing,

<sup>1</sup> Hart, Steenbock, *et al.*: J. Biol. Chem., **77**, 797 (1928).

ship plates, electrotype plates used in printing, coinage, cooking utensils, etc. It is an important constituent of brass, bronze and other alloys.

### COPPER ALLOYS<sup>1</sup>

<i>Alloy</i>	<i>Composition</i>
Aluminum bronze	Copper, 90-98%, aluminum, 2-10%
Brass	Copper, 60-82%, zinc, 18-40%
Bronze	Copper, 70-95%, zinc, 1-25%, tin, 1-18%
Gun metal	Copper, 90%, tin, 10%
Bell metal	Copper, 78%, tin, 22%
German silver	Copper, 56-60%, zinc, 20%, nickel, 20-25%
Nickel coin	Copper, 75%, nickel, 25%
Silver coin	Copper, 10%, silver, 90%
Gold coin	Copper, 10%, gold, 90%
Sterling	Copper, 7.5%, silver, 92.5%

<sup>1</sup> Sneed and Maynard: General Inorganic Chemistry, p. 790.

### OFFICIAL COPPER COMPOUNDS

#### CUPRIC CITRATE

##### *Cupric Citrate, U. S. P. XIII*

Formula, Cu<sub>2</sub>C<sub>6</sub>H<sub>4</sub>O<sub>7</sub>.2½H<sub>2</sub>O. Molecular Weight, 360.27

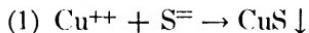
**Physical Properties.**—Cupric Citrate is a green or bluish-green finely crystalline, odorless powder.

It is slightly soluble in water but somewhat more soluble in cold solutions of alkali citrates, forming a greenish-blue solution. It is freely soluble in hot solutions of alkali citrates. Ammonia and dilute acid solutions also dissolve the salt.

**Chemical Properties.**—Cupric citrate loses its water of crystallization at about 100° C. It behaves just as any other organic salt of a metal in that it first chars and then may be ignited to the oxide form (the carbonate is unstable at high temperatures). Its chemical properties are those of copper (*q. v.*) and of the citrate radical (see Sodium Citrate, p. 182).

**Official Tests for Identity.**—1. When dissolved in ammonia T.S., the salt yields an intense blue color due to the formation of the cupric-ammonium ion (*q. v.*).

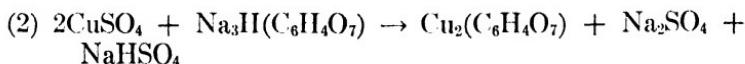
2. If 1 Gm. of the salt is dissolved in 20 cc. of diluted hydrochloric acid, the resulting solution diluted to 200 cc. and treated with hydrogen sulfide, the copper ion is precipitated as sulfide (1).



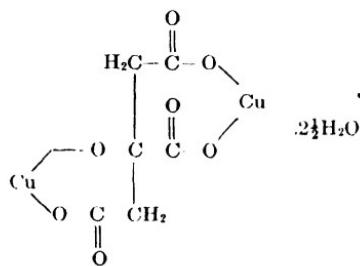
The filtrate from this precipitate will contain citric acid and will respond to all tests for the citrate ion (*q. v.*).

**Commercial Manufacture.**<sup>1</sup>—There is very little published information on the commercial manufacture of cupric citrate. The method of manufacture in current use is based upon original work done by

Kämmerer.<sup>1</sup> Hot aqueous solutions of copper sulfate and sodium citrate are stirred together and allowed to cool. Cupric citrate is formed and crystallizes out. The reaction is said to be the following (2)



The probable structural formula is:



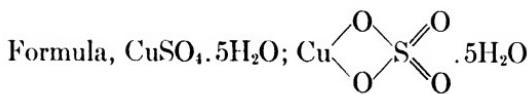
**Laboratory Preparation.**—Dissolve 10 Gm. of Sodium Citrate in 25 cc. of distilled water with the aid of heat. Add this hot solution slowly and with stirring to a hot cupric sulfate solution prepared by dissolving 17 Gm. of Cupric Sulfate in 50 cc. of distilled water. Allow the mixture to cool to room temperature and filter off the precipitate. Wash the precipitate with distilled water until the washings no longer give a test for sulfate ion with barium chloride test solution. Spread out the filter paper and allow the product to dry at room temperature in the dark.

**Pharmaceutical Preparations and Uses.**—1. *Cupric Citrate* (Cupri Citras, Copper Citrate), U. S. P. XIII.—Cupric Citrate is the cupric salt of citric acid and "contains not less than 34 per cent and not more than 37 per cent of Cu, corresponding to not less than 96.3 per cent of  $\text{Cu}_2\text{C}_6\text{H}_4\text{O}_7 \cdot 2\frac{1}{2}\text{H}_2\text{O}$ ." This salt is a new addition to the U. S. P. but has been listed as acceptable by New and Nonofficial Remedies since 1912. It possesses the astringent and mildly antiseptic properties of other salts of copper, but its low solubility minimizes any corrosive effect it might possess. In a 5 to 10 per cent powder (using sugar as a diluent) it has been used externally to treat ulcers, gonorrhea and exuberant granulations. Ten to 20 per cent pencils are available for more convenient application. It has also been used extensively in ophthalmic ointments for the treatment of follicular conjunctivitis and trachoma, usually in a 5 to 10 per cent concentration.

2. *Cupric Citrate Ointment* (Unguentum Cupri Citratis, Copper Citrate Ointment), U. S. P. XIII.—This ointment "contains not less than 7.2 per cent and not more than 8.8 per cent of  $\text{Cu}_2\text{C}_6\text{H}_4\text{O}_7 \cdot 2\frac{1}{2}\text{H}_2\text{O}$ ." It is prepared by incorporating 8 per cent of the finely powdered compound in an ointment base composed of wool fat, light liquid petrolatum and white petrolatum.

<sup>1</sup> Kämmerer, H.: *Annalen*, **148**, 303 (1868); **170**, 186 (1873).

## CUPRIC SULFATE

*Cupric Sulfate*, U. S. P. XIII

Molecular Weight, 249.71

**Physical Properties.**—Cupric Sulfate occurs in the form of deep blue, triclinic crystals of the pentahydrate, or as blue crystalline granules or powder. It effloresces slowly in dry air and the crystals become covered with a white coating of the anhydrous salt. The salt is odorless, and has a nauseous, metallic taste.

One Gm. of cupric sulfate dissolves in 3 cc. of water, in about 500 cc. of alcohol, and very slowly in 3 cc. of glycerin, at 25° C. One Gm. is soluble in 0.5 cc. of boiling water.

**Chemical Properties.**—When heated to 30° C. the salt loses part of its water of crystallization and is converted into a pale blue, amorphous powder composed of a mixture of the several known hydrates (*e. g.*,  $\text{CuSO}_4 \cdot 2\text{H}_2\text{O}$ ;  $\text{CuSO}_4 \cdot 3\text{H}_2\text{O}$ ). At 200° C. it is converted into the white, anhydrous salt. At higher temperatures it is decomposed into sulfur dioxide, oxygen, and black cupric oxide (1).



Copper sulfate, of course, conforms to the chemical properties of its constituent ions, namely the cupric ion and the sulfate ion. This salt is used extensively in the determination of reducing sugars in the form of (1) Fehling's solution and (2) Benedict's solution.

1. Cuprous oxide is precipitated from alkaline solutions of cupric salts when they are boiled with reducing agents, *e. g.*, dextrose and other monosaccharides. Fehling's solution is used for detecting sugars in the urine. *Solution 1*, the copper sulfate solution, and *Solution 2*, the alkaline tartrate solution, are prepared separately and mixed in equal volumes at the time of making the test. *Solution 1* is made by dissolving 34.64 Gm. of crystalline copper sulfate in sufficient distilled water to make 500 cc. at standard temperature. *Solution 2* is made by dissolving 173 Gm. of crystallized potassium and sodium tartrate and 50 Gm. of sodium hydroxide in sufficient distilled water to make 500 cc. at standard temperature. When a portion of *Solution 1* is mixed with an equal volume of *Solution 2*, the copper sulfate and sodium hydroxide probably react to form cupric hydroxide which immediately is converted by the potassium and sodium tartrate into what appears to be a soluble blue-colored compound. It is generally conceded today that the solution probably contains a colloidal form of cupric hydroxide, inasmuch as this assumption explains many of the phenomena connected with the solution. Whatever may be the actual form of the copper in

the solution it is readily converted to cuprous oxide ( $Cu_2O$ ) when heated with a few drops of a solution containing reducing sugars, *e. g.*, diabetic urine. In testing urine it is found that traces of sugar in the urine (0.1 per cent) will only cause a bluish-green coloration of the solution without a precipitate and that with increasing amounts of sugar the color changes gradually to a red accompanied by a precipitate (10 per cent and over).

2. Benedict's solution is used both as a qualitative reagent and as a quantitative solution. The *qualitative* solution contains 17.3 Gm. of crystalline copper sulfate, 173 Gm. of sodium citrate, 117 Gm. of monohydrated sodium carbonate and enough distilled water to bring the volume to 1000 cc. It is used for much the same purpose as Fehling's solution, namely to detect sugar in urine, and the color changes are very similar. It has an advantage over Fehling's solution in that the solution is stable as it is, whereas Fehling's solution must be mixed at the time of use.

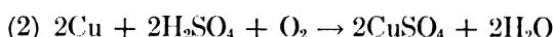
The qualitative reagent should not be confused with the *quantitative* solution which contains 18.0000 Gm. of crystalline copper sulfate (reagent grade), 117 Gm.  $Na_2CO_3 \cdot H_2O$ , 200 Gm. sodium citrate, 125 Gm. potassium thiocyanate, 5 cc. of a 5 per cent potassium ferrocyanide solution and enough distilled water to bring the volume to 1000 cc. The quantitative solution is less commonly used than the qualitative but it is useful for determining the sugar content of urine more accurately than is possible with the qualitative solution.

**Official Tests for Identity.**- 1. Solutions (1 in 20) of cupric sulfate are blue in color.

2. A solution (1 in 10) of cupric sulfate responds to the tests for *Copper* (*q. v.*).

3. A solution also responds to the tests for *Sulfate* (*q. v.*).

**Commercial Manufacture.**- Cupric sulfate is made by roasting copper-bearing sulfide ores in the presence of air, or by heating copper in a furnace with sulfur. The mixture of copper sulfate and copper oxide, obtained by either process, is lixiviated or percolated with dilute sulfuric acid and the resulting solution filtered, concentrated and allowed to crystallize. It is also made by permitting dilute sulfuric acid to trickle over granulated copper in the presence of air (2).



Cupric sulfate may be made by the action of very hot, concentrated sulfuric acid upon copper (3).



**Laboratory Preparation.**- Add 5 Gm. of copper filings to a mixture of 8 Gm. of concentrated sulfuric acid and 4 Gm. of nitric acid contained in a flask. Heat gently at first and gradually raise the temperature to the boiling-point. Boil until the evolution of gas ceases and evaporate the solution to dryness. Dissolve the residue

in four times its weight of water, filter and evaporate to crystallization. Dry the crystals without the aid of heat.

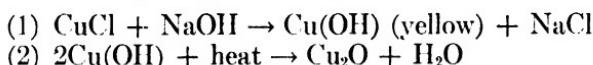
**Pharmaceutical Preparations and Uses.**—*Cupric Sulfate* (Cupri Sulfas, Copper Sulfate), U. S. P. XIII.—This salt should "contain not less than 63 per cent and not more than 66.8 per cent of CuSO<sub>4</sub>, corresponding to not less than 98.5 per cent of the hydrated salt (CuSO<sub>4</sub>. 5H<sub>2</sub>O)." It is also commonly known as "blue vitriol" or "blue stone." Copper sulfate stimulates the vomiting reflex before there is time for any local irritant action. It is not absorbed (except by corroded stomachs) and hence does not produce any systemic effects. The nausea is very short and the after-depression is small. Copper sulfate is used to empty the stomach of indigestible foods and poisons and is of especial value in treating phosphorus poisoning; inactivating the unabsorbed phosphorus particles by forming a coating of metallic copper over them. Copper sulfate is sometimes used on mucous membrane as an astringent and caustic. Despite the fact that it is very toxic to fungi, algae, and protozoa, it is not a reliable bactericide.

Copper sulfate is employed in the textile and leather industries. It is also used in electroplating, in batteries, in copper refining, and in some hair dyes. Its use to prevent the growth of algae in water reservoirs is well known.

A rather novel use of its fungicidal action was noted during World War II. In the South Pacific, copper plating of the feet as a treatment for athlete's foot was successfully used. The treatment takes six minutes and is repeated for six or seven days and requires only a copper plate, copper sulfate solution, and a 6-volt battery.<sup>1</sup>

#### NON-OFFICIAL COPPER COMPOUNDS

**Cuprous Oxide** [Cu<sub>2</sub>O] and **Cuprous Hydroxide** [Cu<sub>2</sub>(OH)<sub>2</sub>].—Cuprous oxide occurs in Nature as the red mineral cuprite (*q. v.*). This dark, carmine red compound is prepared by carefully oxidizing copper powder at gentle heat, or by adding a solution of a fixed alkali to a cold solution of cuprous chloride in hydrochloric acid (1) and then boiling the solution (2).



Cuprous oxide is precipitated from alkaline solutions of cupric salts, *e. g.*, Fehling's solution, when they are boiled with reducing agents such as dextrose and other monosaccharides (see p. 285).

A technical grade is used in the manufacture of red glass, red glazes for porcelain, paint for the hulls of ships, and for treating seeds of some vegetables to control fungus diseases.

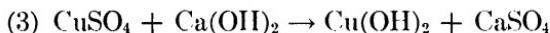
**Cupric Oxide** [CuO] and **Cupric Hydroxide** [Cu(OII)<sub>2</sub>].—Cupric oxide (black) is formed by heating copper in a current of oxygen, or by heating the hydroxide, carbonate or nitrate. It is used in ultimate organic analysis.

Cupric hydroxide (light blue powder) is made by adding a fixed alkali to a solution of a cupric salt (1). The hydroxide reacts with ammonium hydroxide to form a soluble, blue-colored compound (2). This is known as Schweitzer's solution.<sup>1</sup> Cellulose (cotton, paper, wood pulp, etc.) is soluble in a solution of this copper ammonium compound and is precipitated upon the addition of sulfuric acid. Wool is insoluble in Schweitzer's solution. Unsized paper, cotton cloth, etc., may be water proofed by first passing the material through a solution of the copper ammonium compound and then through a bath of dilute sulfuric acid.

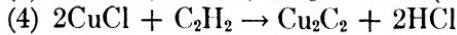
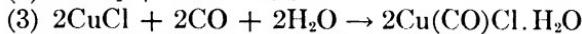
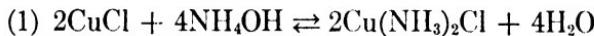


In a similar manner, a concentrated solution of the cellulose copper ammonium compound may be squeezed through capillary tubes into a bath of weak sulfuric acid. The cellulose is precipitated in the form of fine filaments that are known as *artificial silk*.

When milk of lime is added to a solution of copper sulfate, cupric hydroxide is precipitated (3). This mixture (known as Bordeaux Mixture) is used as a spray to prevent or kill the growth of fungi.

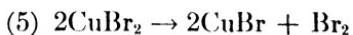


**Cuprous Chloride** ( $\text{CuCl}$ ), **Cuprous Bromide** ( $\text{CuBr}$ ) and **Cuprous Iodide** ( $\text{CuI}$ ).—*Cuprous chloride* is a white, crystalline powder. It is nearly insoluble in water but dissolves in hydrochloric acid to form complex compounds, *e. g.*,  $\text{HICuCl}_2$  and  $\text{H}_2\text{CuCl}_3$ . Hot water rapidly hydrolyzes cuprous chloride to form red, hydrated cuprous oxide. It is soluble in ammonia water giving cuprous ammonium chloride [ $\text{Cu}(\text{NH}_3)_2\text{Cl}$ ] (1) which is quickly oxidized in air to  $\text{Cu}(\text{NH}_3)_4\text{Cl}_2$ . Cuprous chloride melts at  $422^\circ\text{C}$ . and volatilizes at a higher temperature. It is readily prepared by boiling cupric chloride with hydrochloric acid and copper filings (2). The cuprous chloride solution (containing  $\text{HCuCl}_2$ ,  $\text{H}_2\text{CuCl}_3$ ) is heated to expel the air and the cuprous chloride precipitated from the solution by adding freshly boiled water. Cuprous chloride reacts readily with oxygen to form green cuprous oxychloride. With carbon monoxide, it forms an addition product (3), and with acetylene an explosive cuprous acetylide (4). It is used in gas analysis.

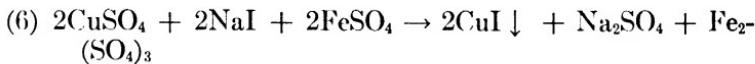


<sup>1</sup> *Cupric Oxide, Ammoniated, Test Solution (Schweitzer's Reagent).*—Dissolve 10 Gm. of cupric sulfate in 100 cc. of distilled water, add sufficient 20 per cent sodium hydroxide solution to precipitate the copper hydroxide, collect the latter on a filter, and wash free from sulfate with cold distilled water. Dissolve the precipitate, which must be kept wet during the entire process, in the minimum quantity of ammonia T.S. necessary for complete solution.

*Cuprous bromide* resembles cuprous chloride in appearance and properties. It is made like the corresponding chloride or, by heating cupric bromide (5).



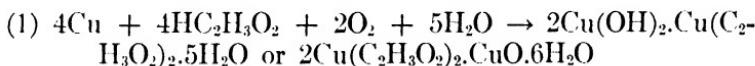
*Cuprous iodide* is precipitated free from iodine by adding solutions of sodium iodide and ferrous sulfate (or sodium thiosulfate, sulfuric acid, sodium sulfite) to a solution of cupric sulfate (6).



**Cupric Chloride** ( $\text{CuCl}_2$ ), and **Cupric Bromide** ( $\text{CuBr}_2$ ).—Cupric chloride may be obtained as a yellow anhydrous salt by allowing chlorine to act upon copper. Green crystals of cupric chloride,  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ , are formed when the solution resulting from the action of hydrochloric acid upon cupric hydroxide or carbonate is slowly evaporated.

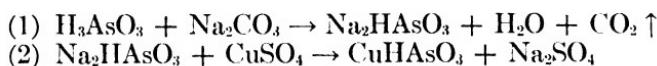
Jet black, deliquescent crystals of *cupric bromide* are obtained by slowly evaporating the solution resulting from the action of bromine water on metallic copper.

**Cupric Acetate** and **Basic Cupric Acetate**.—Basic cupric acetate (green verdigris) is made by oxidizing copper plates in the presence of acetic acid. Sometimes the copper plates are packed alternately in earthen vessels with marc (obtained from wine presses) that has undergone acetic fermentation. The plates become covered with a coating of normal copper acetate, which is converted into the basic salt by moistening and exposing to the air (1).



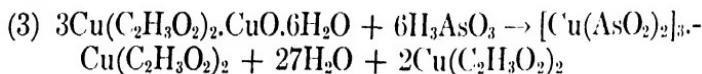
Normal copper acetate,  $\text{Cu}(\text{C}_2\text{H}_3\text{O}_2)_2 \cdot \text{H}_2\text{O}$ , crystallizes in bluish-green crystals having 1 molecule of  $\text{H}_2\text{O}$ . Green verdigris, a greenish-blue powder having 6 molecules of  $\text{H}_2\text{O}$ , is nearly insoluble in water and in alcohol, but it is completely soluble in ammonia solution, in dilute sulfuric, acetic and hydrochloric acids. Its color is not affected by light, hence its use in manufacturing paints. It also is employed in making "Paris green" (*q. v.*).

**Cupric Hydrogen Arsenite** ( $\text{CuHAsO}_3$ ) and **Cupric Acetoarsenite**.—Cupric hydrogen arsenite is known as Scheele's Mineral, or Swedish Green. It is a yellowish-green powder of somewhat variable composition. It is made by adding a solution of sodium carbonate in arsenous acid to a solution of cupric sulfate (1) (2).



Until prohibited by law, it was used to color wall paper. To some extent it is employed as an intestinal antiseptic and as an insecticide.

*Paris, Schweinfurth, Imperial, Vienna, or Parrot Green* is a double salt of the probable formula,  $[\text{Cu}(\text{AsO}_2)_2]_3 \cdot \text{Cu}(\text{C}_2\text{H}_3\text{O}_2)_2$ . It is made by boiling the hot solutions of basic copper acetate and arsenous acid (3).



It is used as an insecticide.

## CHAPTER XVI

### SILVER AND SILVER COMPOUNDS

#### SILVER

##### *Argentum*

Symbol, Ag. Valence, 1. Atomic Weight, 107.88;  
Atomic Number, 47

**History and Occurrence.**—Silver has been known from the earliest times. It is of great importance as a “noble” metal because of its use in making articles of value, *e. g.*, coins, ornaments and jewelry. The name *silver* is derived from the Anglo-Saxon word *seolfor*. The Latin *Argentum*, from which the symbol Ag is taken, is allied with the Greek  $\alpha\rho\gamma\psi\rho\sigma$ , silver, which in turn is derived from  $\alpha\rho\gamma\delta\sigma$ , shining. The alchemists named it *Luna* and characterized it by the crescent moon. The name *Luna* has survived in *Lunar caustic* (silver nitrate).

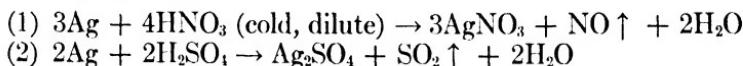
Silver occurs widely distributed in Nature, the principal supplies coming from Mexico, United States, and Australia. Native silver is found in metalliferous veins, where it has been formed presumably by the reduction of silver sulfides or other silver-bearing minerals. Silver is also found as an amalgam and as alloys with gold, platinum, copper, and other metals. It occurs combined with tellurium in the minerals *hessite* [Ag<sub>2</sub>Te], *petzite* [(AgAu)<sub>2</sub>Te], and *sylvanite* [AuAg<sub>3</sub>Te<sub>4</sub>]. As the sulfide [Ag<sub>2</sub>S], silver is found in the minerals *argentite* and *acanthite*. In the form of the double sulfides of antimony or arsenic, silver occurs in the minerals, *pyrargyrite* [3Ag<sub>2</sub>S.Sb<sub>2</sub>S<sub>3</sub>], *proustite* [3Ag<sub>2</sub>S.As<sub>2</sub>S<sub>3</sub>], *polybasite* [9Ag<sub>2</sub>S.Sb<sub>2</sub>S<sub>3</sub>] and *pearceite* [9Ag<sub>2</sub>S.As<sub>2</sub>S<sub>3</sub>]. Silver is found combined with the respective halogens in the minerals *cerargyrite* or *horn-silver* [AgCl], *bromyrite* [AgBr], and *iodyrite* [AgI].

**Physical Properties.**—Pure silver is a white metal having a metallic luster. With the exception of gold it is the most malleable and ductile of all the metals. Its specific gravity is about 10.5 and its hardness is greater than gold but less than copper. It melts at 960.5° C. and boils at about 1950° C. Molten silver occludes about 22 volumes of oxygen which is not permanently retained. On cooling it is given off with great violence. This phenomenon is called the “spitting” or “sprouting” of silver and causes the silver to form in irregular masses. Silver is the best conductor of electricity.

**Chemical Properties.**—The chemical properties of silver may be conveniently discussed under the headings: (1) metallic silver, and (2) silver ion.

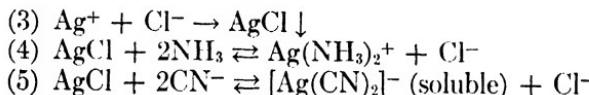
1. Under ordinary conditions silver is not oxidized by oxygen, but like mercury, it is oxidized by ozone. On heating, silver combines

with free halogens and with sulfur. Black silver sulfide is formed when silver comes in contact with substances containing sulfur, *e. g.*, coal-gas, eggs, rubber, perspiration, etc. Because the metal stands below hydrogen in the electromotive series it does not displace hydrogen from acids, but it is attacked by the oxidizing acids (see also Copper, p. 278), *e. g.*, nitric acid (1) and hot sulfuric acid (2). To make solutions of silver for testing purposes, nitric acid is the proper solvent to use.



2. Silver forms only one series of salts, the monovalent silver ion ( $\text{Ag}^+$ ) being the form in which it exists. Most of the silver salts are insoluble, but there are a few soluble ones, namely, the nitrate, sulfate, chlorate, nitrite, acetate and a few others. Exposure to sunlight of silver salts either in the solid state or in solution results in a darkening of the material because of reduction to free silver.

When hydrochloric acid or a solution of a soluble chloride is added to a neutral or acid solution of a silver compound, a white, curdy precipitate of silver chloride is produced (3), which is insoluble in dilute acids, but soluble in ammonium hydroxide (4) and in potassium cyanide solution (5).

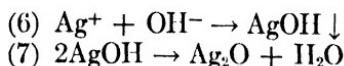


The solubility of silver chloride in ammonium hydroxide is due to the formation of the complex silver ammonia cation (5). This is due to the fact that silver chloride ionizes to a greater extent than does the complex ion (in an excess of ammonium hydroxide) and, therefore, silver ions are "used up" in the formation of the complex ion causing the  $\text{AgCl}$  to go into solution. In a normal solution of ammonia in which silver chloride has been dissolved it is found that there are 10,000,000 complex ions to every simple silver ion ( $\text{Ag}^+$ ).

On the other hand, it is found that while silver ion is precipitated by bromides and iodides to give insoluble silver bromide and silver iodide, these precipitates are insoluble in an excess of ammonium hydroxide. The reason for this is that the bromide and iodide do not ionize to furnish silver ions to as great an extent as does the complex ion and, therefore, they cannot go into solution by the mechanism outlined for silver chloride. However, potassium cyanide dissolves all of the silver halides and the mechanism is exactly the same as that for ammonium hydroxide except that the silver cyanide anion is formed (5) instead of the silver ammonia cation.

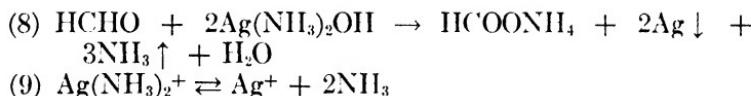
Soluble silver salts react with alkali hydroxides to form silver hydroxide (6) which immediately decomposes to brown silver oxide (7). In this case, the precipitate is insoluble in excess alkali

hydroxide because no complex ion is formed, but it is soluble in nitric acid and ammonia.



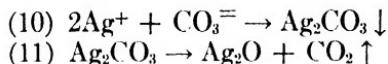
Careful addition of ammonium hydroxide to a solution of a silver salt results in exactly the same kind of precipitate as with the alkali hydroxides (6, 7), but excess ammonia, of course, dissolves the precipitate for reasons previously mentioned.

If ammonium hydroxide is added to a solution of a silver salt, *e. g.*, silver nitrate, most of the silver ions in the solution are converted to the silver-ammonia complex. This leaves relatively few silver ions in the solution. If to this solution is then added a reducing agent such as formaldehyde, glucose, etc., the free silver ions are reduced to the metallic state (8) and form a "silver mirror" on the walls of the container. As the silver ions are being converted to metallic silver the equilibrium between the silver-ammonia complex and silver ions (9) is disturbed and more silver ions are gradually liberated until all of the silver from the complex ion is deposited as the metal.



In commercial solutions used for electroplating it is common practice to use a bath containing the silver-cyanide complex since this has even fewer silver ions in equilibrium with it than the silver-ammonia complex. The object to be plated acts as a cathode and silver metal is the anode in these plating baths. The fact that there is such a low concentration of silver ions in the solution is the principal reason why silver is plated out in such fine crystals on the surface of the object to be plated.

Addition of sodium carbonate to solutions of silver salts causes precipitation of white silver carbonate (10) which can be decomposed by boiling to give silver oxide (11).



Numerous other salts of silver are precipitated on the addition of suitable reagents, *e. g.*, sodium phosphate, sodium thiosulfate, etc.

Addition of silver nitrate solution, for example, to a protein solution causes the formation of a heavy precipitate of a complex protein-silver compound. Although this reaction is not well defined it is the basis of much of the medicinal efficiency of silver salts.

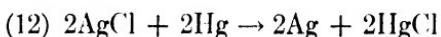
**Official Tests for Silver Ion.**—1. Solutions of silver salts will give a white, curdy precipitate of silver chloride when treated with hydrochloric acid (3). The precipitate is soluble in excess ammonia T.S. (4), but is insoluble in nitric acid.

2. An ammoniacal solution of a silver salt when treated with a small quantity of formaldehyde and warmed, causes the formation of a silver mirror on the walls of the test-tube (8).

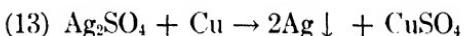
**Commercial Manufacture of Silver.**—A number of processes have been devised for obtaining silver from its ores. They vary according to the chemical composition of the ores to be worked.

✓ *Amalgamation Process.*—As previously indicated, silver readily forms an amalgam. Some silver ores containing free silver or silver chloride may be finely powdered and then extracted with mercury. The amalgam is washed free of powdered rock and the mercury recovered by distillation in an iron retort. The remaining retort silver is then cast into bars and shipped to a refinery.

Certain complex silver minerals (pyrargyrite, proustite, etc.) are very difficult to amalgamate and hence must be made amenable to such a process. This is accomplished by either the flotation process (see p. 280) or by converting the metal in the ore to silver chloride and sulfate by roasting with about 10 per cent of sodium chloride. The volatile arsenic and antimony chlorides are expelled during the roasting of the ore. When the mixture of silver chloride, silver sulfate, rock, etc., is treated with mercury, the chloride and sulfate are reduced to metallic silver (12) which combines at once with the mercury to form an amalgam.



*Lixiviation or Leaching Process.*—When simple silver sulfide ores are roasted, the sulfide is converted into soluble silver sulfate which is dissolved from the mass with water. Scrap copper now is added to the solution in order to precipitate the silver (13).



✓ *Cyanide Process.*—In this process silver ores are treated with sodium cyanide to solubilize the compounds of silver as the silver cyanide complex (see Chemical Properties). The silver is obtained from the silver cyanide complex by displacing it with zinc, or by precipitating it as the sulfide through the addition of sodium sulfide.

Silver is also obtained from the sludge formed in the electrolytic refining of copper (p. 281). Lead ores usually contain small quantities of silver, which may be recovered by the *Parke process*. This process is based upon the principle of "selective solvents" or "partition" (see footnote). It will be noted that molten lead and zinc are nearly insoluble in one another whereas molten silver is much more soluble in molten zinc than in molten lead. The lead is melted and thoroughly mixed with a small quantity of zinc. The zinc-silver alloy, being lighter than lead, soon comes to the top, solidifies as a crust over the molten lead and may be lifted off. The "crust" is then melted and the adhering lead drained off from

**NOTE:** At a given temperature and pressure, the proportionate distribution of a pure solute in solution in two immiscible solvents is constant.

the bottom. Zinc, being the more volatile of the two metals, is distilled off in clay retorts. The silver still contains a small amount of lead which is removed by *cuppellation*. The melted alloy of silver and lead is strongly heated in an air blast, whereby the lead is oxidized to litharge ( $PbO$ ) and may be skimmed off. Gold is usually present in the silver obtained in this manner. It is separated electrolytically. The silver-gold alloy is cast into plates that serve as the anodes. A solution of silver nitrate is the electrolyte. Silver, being the more active of the two metals is ionized and deposits upon the cathode, whereas the gold collects in a bag around the anode. (See Electrolytic Refining of Copper, p. 281).

**Pharmacology of the Silver Ion.**—Silver ion, in common with other heavy metals is a protein precipitant and, because it makes no distinction between bacterial and human protein it has a high germicidal efficiency. The action of silver ion on tissue may be said to be antiseptic, astringent, irritant or corrosive, depending upon the concentration of free silver ion on the tissue.

As a rule, the irritant and corrosive effects are desired only when it is wished to destroy tissue or stimulate slow healing wounds. For this purpose, the more highly ionized silver salts, *e. g.*, silver nitrate, are used exclusively. Because of the precipitation of the silver ion by proteins and chlorides in the tissues this irritant and corrosive effect is easily localized.

Although accompanied by some protein precipitation and silver chloride formation, dilute solutions of silver salts such as silver nitrate may be used for astringent and antiseptic effects and, indeed, are required for the astringent action. However, the antiseptic effect may be obtained with less highly ionized substances, namely, the silver halides and silver proteinates. The mechanism of action of these substances is exactly the same as that of the so-called "late action" of silver nitrate. When silver nitrate is applied to the tissues it, of course, gives the immediate irritant and corrosive effect (also highly germicidal). After that effect has passed, however, the precipitated proteins and chlorides begin to redissolve and ionize off small amounts of silver ion. This small amount of silver ion exerts a definite antiseptic action. Therefore, rather than applying silver nitrate to obtain the antiseptic action it is more desirable to apply the silver proteinate or halide as such. This avoids the formation of a coagulation membrane which may hinder the action and likewise may eliminate the pain accompanying silver nitrate application.

In view of the above statements a distinction may be made between two principal types of silver salts which are used therapeutically:

1. Highly ionized silver salts, *i. e.*, silver nitrate, silver picrate, etc.
2. Slightly ionized silver salts, *i. e.*, silver halides, silver proteinates (*mild* and *strong*, depending on amount of ionized silver and not on total per cent), etc. These are usually referred to as the "colloidal silver preparations."

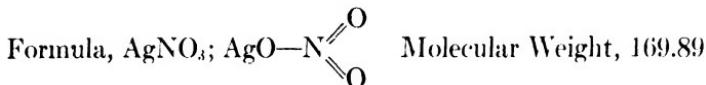
The internal use of silver salts results in no systemic action because of the readiness with which the silver is precipitated, and for this reason silver salts are not used for internal medication.

Whenever silver preparations are used for long periods of time they are apt to cause a discoloration of the skin (darkening) called "argyria" which is probably due to deposition of free silver in the skin. This condition is irremediable, although it is said that injection of a solution of 6 per cent sodium thiosulfate and 1 per cent potassium ferricyanide subcutaneously will remove the color. However, this treatment requires innumerable small injections into the area involved and if the area is extensive the difficulties can be appreciated.

#### OFFICIAL COMPOUNDS OF SILVER

##### SILVER NITRATE

*Silver Nitrate, U. S. P. XIII*



**Physical Properties.**—Silver Nitrate occurs as colorless or white, odorless, rhombic crystals, commonly tabular, having a bitter, caustic, metallic taste. It has a density of about 4.35. When pure, the salt is not affected by light. However, in the presence of organic matter (skin, cloth, etc.) and light it soon becomes gray or grayish-black due to liberated silver, hence its use in marking-inks.

One Gm. of Silver Nitrate dissolves in 0.4 cc. of water and in 30 cc. of alcohol, at  $25^{\circ}\text{C}$ . One Gm. of the salt is soluble in slightly more than 0.1 cc. of boiling water and in 6.5 cc. of boiling alcohol. It is slightly soluble in ether.

At  $212^{\circ}\text{C}$ . the salt melts to a slightly yellow liquid which, on cooling, congeals to a white crystalline mass. At higher temperatures it slowly decomposes, evolving oxides of nitrogen.

**Chemical Properties.**—Silver nitrate embodies the chemical reactions of the silver ion (*q. v.*) and the nitrate ion (*q. v.*).

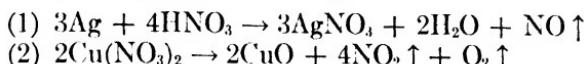
Aqueous solutions are neutral to litmus paper.

**Official Tests for Identity.**—1. A 1 in 50 solution responds to all tests for the *Silver ion* (*q. v.*).

2. When a 1 in 10 solution of silver nitrate is mixed with a drop of diphenylamine T.S. and then carefully superimposed on concentrated sulfuric acid, a blue color appears at the interface of the two layers. This test is the "Lunge test" and is a sensitive test for the nitrate ion, but is also a sensitive test for a number of other oxidizing agents, *e. g.*, nitrous acid, ferric chloride, etc.

**Commercial Manufacture.**—About 3 parts of metallic silver are mixed in a large porcelain dish with 10 parts of 25 per cent nitric acid. If necessary, the mixture is gently warmed to hasten the

reaction (1). When the silver is dissolved, the solution is filtered through glass-wool and evaporated to dryness on a sand-bath. The temperature is then raised to fusion and any cupric nitrate present is converted into insoluble oxide (2). The fused mass is then dissolved in double its weight of water, filtered, and set aside in a dark, dust-proof room to crystallize.



**Pharmaceutical Preparations and Uses.**—1. *Silver Nitrate* (Argenti Nitras), U. S. P. XIII.—“Silver Nitrate, when powdered and dried in the dark over sulfuric acid for 4 hours, contains not less than 99.8 per cent of  $\text{AgNO}_3$ .” Depending on the concentration of its solution, silver nitrate may be used for effects that vary from a caustic effect to that of an antiseptic. It is routinely used in the form of a 1 per cent solution as an instillation in the eyes of newborn babies. For this use the dose is 1 drop in each eye and it is used to guard against *ophthalmia neonatorum*.<sup>1</sup> The use of silver nitrate on tender mucous membranes even in dilute solution is not as popular as it was at one time. This is due largely to the advent of the colloidal silver preparations and various other less irritant medications. However, the use of the “silver nitrate pencil” (see Toughened Silver Nitrate) has been retained to some degree for removing warts and other skin excrescences and as an application to the so-called “canker sores” in the mouth.

The removal of silver nitrate stains from the skin and clothing sometimes is a problem for the pharmacist. According to a U. S. D. A. bulletin,<sup>2</sup> stains may be removed from the skin by painting the places with tincture of iodine and then removing this with ammonia water. Stains from the clothing may sometimes be removed by the judicious use of potassium cyanide, the operator constantly keeping in mind the poisonous character of the cyanide.

2. *Toughened Silver Nitrate* (Argenti Nitras Induratus, Moulded Silver Nitrate, Fused Silver Nitrate, Silver Nitrate Pencils, Lunar Caustic), U. S. P. XIII.—“Toughened Silver Nitrate contains not less than 94.5 per cent of  $\text{AgNO}_3$ .” This preparation is a white, hard, crystalline, odorless solid usually in the form of pencils or cones. It becomes gray or grayish-black on exposure to light due to formation of free silver. Lunar caustic is usually made by adding to silver nitrate about 4 per cent of its weight of hydrochloric acid, melting the mixture at as low a temperature as possible and casting in silver moulds. The presence of about 5 per cent of silver chlorides toughens the silver nitrate and thus lessens the friability of the pencils. As indicated under Silver Nitrate, it is used for local application.

3. *Ammoniacal Silver Nitrate Solution* (Liquor Argenti Nitratis Ammoniacalis; Ammoniacal Silver Nitrate, Howe), N. F. VIII.—

<sup>1</sup> Lehrfeld, J.A.M.A., 135, 306, (1947).

<sup>2</sup> U. S. D. A. Bulletin No. 1474.

This is an aqueous solution of silver diammino nitrate, containing in each 100 Gm. the equivalent of not less than 28.5 Gm. and not more than 30.5 Gm. of silver (Ag), and not less than 9 Gm. and not more than 9.7 Gm. of ammonia ( $\text{NH}_3$ ).

The silver nitrate (70.4 Gm.) is powdered in a glass mortar and dissolved in 24.5 cc. of distilled water, warming if necessary. The solution is cooled to room temperature and Strong Ammonia Solution added from a burette until all but the last trace of black precipitate is dissolved (3).



This last trace of precipitate is filtered from the solution. This dental preparation should be preserved in small glass-stoppered containers, or in ampuls, and protected from light. For oral use—mix Ammoniacal Silver Nitrate Solution with a reducing agent, such as 10 per cent formaldehyde or eugenol, so as to deposit the metallic silver in the infected area in a state of fine subdivision.

### MILD SILVER PROTEIN

*Mild Silver Protein*, U. S. P. XIII

Formula, Indefinite

**Physical Properties.**—Mild Silver Protein occurs as dark brown or almost black, odorless shining scales or granules. It has a tendency to be hygroscopic. It is freely soluble in water, but almost insoluble in alcohol, chloroform and ether. The material and its solutions are prone to decompose upon exposure to light and consequently should be well protected.

**Chemical Properties.**—Mild Silver Protein is a preparation which forms a colloidal solution when dissolved in water. It contains very little free silver ion. Some believe that even in the case of the mild silver protein, silver chloride is formed upon contact with chlorides (*e. g.*, perspiration, tears, etc.) but is held in colloidal suspension by the very nature of the preparation.

**Official Tests for Identity.**—1. A small amount of the preparation is ignited to remove all organic material and the residue is dissolved in nitric acid. The diluted nitric acid solution yields a precipitate of silver chloride when treated with a few drops of hydrochloric acid. The silver chloride precipitate is soluble in ammonia T.S.

2. Addition of ferric chloride T.S. to a 1 in 100 solution of Mild Silver Protein discharges the dark color and gradually produces a precipitate.

3. Addition of a few drops of mercury bichloride to 10 cc. of a 1 in 100 solution of Mild Silver Protein causes the formation of a white precipitate together with a nearly colorless supernatant liquid.

4. It gives no turbidity in a 1 to 100 solution on addition of a 1 to 100 solution of sodium chloride.

**Commercial Manufacture.**—The procedure for preparing Mild Silver Protein is not a standardized one. In general, commercial preparations of this kind are manufactured by a process which involves the reduction and subsequent "solution" of silver or silver oxide, or some silver-protein precipitate, in an excess of denatured protein (made by destroying the complement by electrolysis or by heating to 56° C.) and drying *in vacuo*. The difference in methods of manufacture is well illustrated by the fact that not only do preparations of the different manufacturers have a different ionizable silver content (the criterion for antiseptic efficiency) but even different lots made by the same manufacturer vary in the silver content.

**Pharmaceutical Preparations and Uses.**—1. *Mild Silver Protein* (Argentum Proteinicum Mite, Mild Protein Silver, Mild Protargin), U. S. P. XIII.—"Mild Silver Protein is silver rendered colloidal by the presence of, or combination with, protein. It contains not less than 19 per cent and not more than 23 per cent of Ag." The U. S. P. cautions, "*Solutions of Mild Silver Protein should be freshly prepared and should be dispensed in amber-colored bottles.*" This preparation is practically non-irritant and may be applied to tender mucous membranes with impunity, although continued application may result in "argyria." It is used in aqueous solution in concentrations from 5 to 25 per cent as a mild antiseptic in the eye, ear, nose and throat. It is interesting to note that while this preparation actually contains more silver than the Strong Protein Silver it yields less ionized silver and for this reason is termed "mild." Some of the commercial preparations which fall into this category are *Silvol* (Parke, Davis), *Solargentum* (Squibb), *Argyn* (Abbott), and *Argyrol* (Barnes).

### COLLOIDAL SILVER CHLORIDE

#### *Colloidal Silver Chloride, N. F. VIII*

Formula, AgCl plus a colloid stabilizing agent

**Physical Properties.**—Colloidal Silver Chloride occurs as a white slightly hygroscopic, granular powder with a sweetish, metallic taste. It is easily dispersed in water, forming an opalescent suspension of variable color depending on the light. It is affected by light and accordingly should be protected in light-resistant containers.

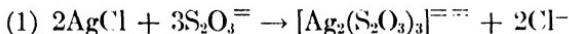
**Chemical Properties.**—In contact with water silver chloride ionizes to a slight extent. A saturated solution at 25° C. has a solubility product of  $1.56 \times 10^{-10}$  which, therefore, indicates a molar concentration of  $1.25 \times 10^{-5}$  silver ions. The AgCl content may be precipitated by acidifying an ammoniacal solution of the preparation with nitric acid.

**Official Tests for Identity.**—1. Addition of 0.6 Gm. of KI dissolved in 3 cc. of distilled water to 25 cc. of an aqueous solution of the

preparation (1 in 50) causes the formation of a yellow color. The color is due to the formation of small amounts of insoluble silver iodide.

2. A clear solution is obtained upon the addition of 8 cc. of strong ammonia solution to 25 cc. of a 1 in 5 aqueous solution of Colloidal Silver Chloride. As previously shown, this is due to the formation of the water-soluble silver-ammonia complex.

3. A clear, colorless solution is obtained upon the addition of 15 cc. of sodium thiosulfate T.S. to a 1 in 20 solution of Colloidal Silver Chloride. In this case the thiosulfate acts in a manner exactly analogous to ammonia and cyanide by forming a water-soluble complex silver ion (1).



**Commercial Manufacture.**—This preparation is made by reducing silver chloride to a colloidal state of subdivision and then rendering the chloride colloidal by the use of 90 per cent of sugar (sucrose) or other suitable agent.

**Pharmaceutical Preparations and Uses.**—1. *Colloidal Silver Chloride* (Argenti Chloridum Colloidale), N. F. VIII.—“Colloidal Silver Chloride is silver chloride rendered colloidal by the presence of sucrose or other suitable colloid stabilizing agent. It contains not less than 9 per cent and not more than 11 per cent of AgCl.” The prototype of this preparation was Lunosol (Hille Labs.) although Lunosol is marketed as a liquid preparation. This material is used “for prophylaxis against and treatment of infections of the accessible mucous membranes, such as the genito-urinary tract and the eye, ear, nose and throat” (N. N. R. 1947). It is used in concentrations of from 3 to 100 per cent as determined by the indications.

### COLLOIDAL SILVER IODIDE

#### *Colloidal Silver Iodide*, N. F. VIII

Formula, AgI plus a colloid stabilizing agent

**Physical Properties.**—It consists of pale yellow granules. They are soluble in water up to 50 per cent and form a colorless, milky, or opalescent solution. It is slowly soluble in glycerin but insoluble in fixed oils. Aqueous solutions of the preparation are best made by adding the total amount of Colloidal Silver Iodide to the water and shaking vigorously for one minute.

**Chemical Properties.**—Silver iodide ionizes even less than does silver chloride when in a saturated solution. Its solubility product is  $1.5 \times 10^{-16}$ , corresponding to a silver-ion content of  $1.25 \times 10^{-8}$  moles per liter. The colloidal solution may be destroyed by boiling an acidified solution (HCl) to precipitate the silver iodide.

**Official Tests for Identity.**—1. Two cc. of sodium hydroxide T.S. are added to 5 cc. of an aqueous solution of Colloidal Silver Iodide

(1 in 100) and upon boiling, the solution darkens but does not form a precipitate inside of ten minutes.

2. Addition of 1 cc. of diluted hydrochloric acid to 5 cc. of a 1 in 100 solution of the preparation causes the solution to become opaque. It must be boiled for one minute, however, to precipitate the silver iodide.

**Commercial Manufacture.**—Silver iodide is rendered colloidally stable by the use of gelatin. As is the case in many of these colloidal preparations the gelatin acts as a barrier between the various colloidal particles preventing them from coming together to form larger particles.

**Pharmaceutical Preparations and Uses.**—1. *Colloidal Silver Iodide* (Argenti Iodidum Colloidale), N. F. VIII.—“Colloidal Silver Iodide is silver iodide rendered colloidally stable by the presence of gelatin. It contains not less than 18 per cent and not more than 22 per cent of AgI.” The N. F. cautions that “*Solutions of Colloidal Silver Iodide should be freshly prepared and should be dispensed in amber-colored bottles.*” It is used the same as other colloidal silver preparations, *viz.*, in concentrations ranging from 2 per cent for irrigating sinuses to 50 per cent in the female genital tract.

## STRONG PROTEIN SILVER

### *Strong Protein Silver, N. F. VIII*

Formula, Indefinite

**Physical Properties.**—It occurs as a pale yellowish-orange to brownish-black, odorless powder. It is usually somewhat hygroscopic and is affected by light. Strong Protein Silver is freely soluble in water, but is best prepared by dusting on the surface of the water and allowing to slowly dissolve in that manner. It is almost insoluble in alcohol, chloroform, and in ether.

**Chemical Properties.**—Strong Protein Silver is capable of liberating more silver ion than Mild Silver Protein, although it also is a colloidal preparation.

**Official Tests for Identity.**—1. When a small sample is ignited to remove all organic matter and the residue dissolved in nitric acid, the acid solution yields a precipitate of silver chloride when treated with hydrochloric acid.

2. Addition of a solution of sodium chloride produces no turbidity, *i. e.*, no silver chloride formation.

3. Ferric chloride discharges the dark color and gradually produces a precipitate. Ferric ion is a good protein precipitant.

4. Mercuric chloride added to a solution of the salt produces a white precipitate with a colorless supernatant liquid. Mercuric ion is even more effective as a protein precipitant than silver.

**Commercial Manufacture.**—This type of preparation varies also with the manufacturer just as was found with the Mild Silver Protein. Protargol (a representative preparation) is said to be

prepared by precipitating a "peptone" (albumose) solution with silver nitrate or with moist silver oxide; dissolving the silver peptone in an excess of protalbumose; and drying *in vacuo*. (N. N. R., 1947.)

**Pharmaceutical Preparations and Uses.**—1. *Strong Protein Silver* (Argentum Proteinicum Forte, Strong Silver Protein, Strong Protagin), N. F. VIII.—"Strong Protein Silver contains not less than 7.5 per cent and not more than 8.5 per cent of Ag." The N. F. cautions "*Strong Protein Silver Solutions should be freshly prepared and should be dispensed in amber-colored bottles.*" This preparation liberates more silver ions than does the Mild Silver Protein, but it contains at the same time less actual silver. It has a much stronger germicidal action than has the mild silver protein. Prior to the advent of the sulfonamides it was extensively used with more or less satisfactory results as an aqueous solution for urethral injection in the treatment of gonorrhea. It should be constantly remembered that preparations of this type are prone to cause argyria.

#### NON-OFFICIAL SILVER COMPOUNDS

**Silver Bromide** (AgBr).—Silver bromide is found as the mineral bromargyrite or bromyrite in Mexico and Chile. The salt is obtained as a pale yellow precipitate when a solution of a bromide is added to a solution of a silver salt. Its specific gravity is 6.47. It is even more insoluble than the chloride (0.000026 Gm. dissolves in 100 cc. H<sub>2</sub>O at 25° C.). It melts at 432° C. When exposed to light it behaves like the chloride and hence is used in photography. The various steps involved in producing a photograph are as follows:

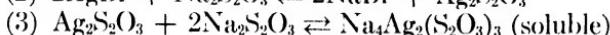
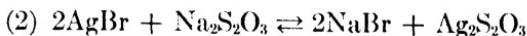
1. Glass plates or celluloid sheets are covered with an emulsion of gelatin in which silver bromide is suspended. These sensitized plates or films are arranged in a camera or Kodak and by means of a "finder," the image of the object to be photographed is focussed on one of them.

2. The exposure is made through lenses of various designs and the time is controlled by an automatic-time, diaphragm shutter. The length of time necessary to give the best results differs according to the time of day and nature (water, shade, sunlight) of the object.

3. The exposed plate is removed from the camera in a dark-room and must be developed. All of the silver bromide on the plate will be reduced to metallic silver if the "developer" [an alkaline solution of pyrogallol, hydroquinone (potassium salt)] (1) is allowed to remain too long in contact with the plate. However, the parts of the halide affected by light are acted upon *first* and with a speed that is proportional to the intensity of the illumination that reached the plate at every point.

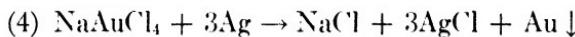


4. When the desired "development" is attained the plate is immersed in a "fixing" bath consisting of a solution of sodium thiosulfate (hypo). The unreduced silver bromide is dissolved by the thiosulfate (2) (3) and only a thin silver coating corresponding to the image remains on the plate. The wet plate is washed and dried and is known as a *negative*.



5. The print is made by placing the *negative* over a sheet of sensitized paper and exposing it to light. Here again the light and dark parts are reversed; the fixed silver particles protecting the compounds on the paper from the light. Printing papers containing silver bromide require only short exposure and are developed like the plate. When silver chloride is the sensitive substance, the paper must be exposed to the light through the negative for some time. They must then be "fixed" by treating with a solution of sodium thiosulfate (see 2).

6. After "fixing" the print may be *toned* by displacing some of the silver deposit with gold (4). A solution of sodium chloraurate is employed for this purpose and gives a reddish brown tone or color to the print.



Steel-gray tones may be obtained by using a platinum solution.

In addition to its use in photography, silver bromide has been marketed at least by one firm as a colloidal preparation very similar to the official colloidal preparations of silver halides and is used for much the same purposes.

**Silver Oxide** ( $\text{Ag}_2\text{O}$ ).—Silver oxide is obtained as a dark brown, amorphous precipitate when a fixed alkali hydroxide is added to a solution of silver nitrate. At  $300^\circ \text{ C}$ . it decomposes rapidly into silver and oxygen, and when triturated with organic matter may cause an explosion. Aqueous solutions of silver oxide (0.00215 Gm.  $\text{Ag}_2\text{O}$  dissolved in 100 cc.  $\text{H}_2\text{O}$  at  $20^\circ \text{ C}$ .) are decidedly alkaline. This alkalinity is evidently the result of the formation of some silver hydroxide (5).



Silver oxide is an active, basic oxide. When moistened, it readily absorbs carbon dioxide from the air. "*Hopcalite*" is a mixture of colloidal manganese and copper oxides activated by silver and cobalt oxide and is capable of oxidizing carbon monoxide to dioxide at ordinary temperatures. This mixture is a product of the Chemical Warfare Service, U. S. A., and is used not only in the canister of the "miner's self-rescuer" but also in gas masks for firemen and others who are subjected to dangerous concentrations of carbon monoxide. It is used particularly in artillery masks to protect against carbon monoxide.

**Silver Picrate** (Picragol, Pierotol), Silver Trinitrophenolate— $C_6H_2(OAg)(NO_2)_3 + H_2O$ , N. N. R. 1947.—Silver picrate occurs as yellow crystals which are sensitive to sunlight. They are soluble to the extent of about 2 Gm. to 100 cc. of water, sparingly soluble in alcohol, slightly soluble in acetone and glycerin and practically insoluble in chloroform and ether.

The silver is readily precipitated as the chloride from this compound when it is dissolved in water.

Silver picrate is used similarly to the other simple silver salts that are more or less highly ionized. It is used in a dilution of approximately 1 to 2 per cent for its antiseptic action and has been marketed (Wyeth) in the form of a compound powder for use in the treatment of *Trichomonas vaginalis* and *Monilia albicans*, as a vaginal suppository for much the same indications, and also as the pure crystals for urethritis, etc.

**Other Salts of Silver.**—Silver ion is precipitated by a number of anions and gives salts that for the most part may be considered as insoluble. (See Table.)

Name	Formula	Color	Form; M.P.	
Silver arsenate	$Ag_3AsO_4$	Dark brown	Solid reg.	None
Silver arsenite	$Ag_3AsO_3$	Yellow	Solid, decomp. 150°C.	None
Silver carbonate	$Ag_2CO_3$	Light yellow, darkened by light	Crystalline solid, de- comp. 220°C.	None
Silver chromate	$Ag_2CrO_4$	Brick-red	Crystalline powder	None
Silver cyanide	$AgCN$	White or grayish	Amorphous powder, decomp. 320°C.	Formerly used to make U.S.P. VIII Diluted Hydrocyanic Acid
Silver metaphosphate	$AgPO_3$	White	Solid, 482° C.	None
Silver orthophosphate	$Ag_3PO_4$	Yellow— darkens	Solid, 849° C.; Reg.	None
Silver sulfide	$Ag_2S$	Black	Amorphous solid, 823° C.; Rhombic	None

## CHAPTER XVII

### GOLD AND GOLD COMPOUNDS

#### GOLD

##### *Aurum*

Symbol, Au. Valence, I, III. Atomic Weight, 197.2;  
Atomic Number, 79

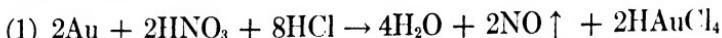
**History and Occurrence.**—Since the earliest times, gold has been recognized as the “king of all metals.” Because of its color, scarcity, and permanency in contact with the atmosphere, it has been valued from the earliest ages for making jewelry, coins, etc. The symbol, Au, is derived from its Latin name, *Aurum*. Ornaments of great variety and elaborate workmanship have been discovered in ruins belonging to the earliest known civilizations, *rīz.*, Minoan, Egyptian, Assyrian, Etruscan, etc. In ancient literature, it was the universal symbol of highest purity and value. No doubt because of its yellow color, the alchemists associated gold with the sun.

Gold is found widely but sparingly distributed in Nature. It occurs principally as the metal *per se*, or alloyed with other metals, such as lead, copper and silver. The free metal occurs mixed with alluvial sand. Gold alloys are found disseminated in veins of quartz. Associated with tellurium, small quantities occur with the sulfide ores of copper, iron and lead. The principal minerals containing the double telluride of gold and silver are *sylvanite* [Au Ag<sub>2</sub>Te<sub>4</sub>], *petzite* [(Au Ag)<sub>2</sub>Te] and *calaverite* [Au Te<sub>2</sub>]. The Transvaal of South Africa and the United States (California and Colorado) lead in gold production. Other great gold producing centers are Alaska, British Columbia, Australasia, Canada, India, China, Russia and Mexico.

**Physical Properties.**--Gold has a yellow color, which is lowered by small quantities of silver, but heightened by copper. Gold that has been beaten into a thin leaf transmits a greenish light. It is the most malleable and ductile metal known. When pure, it is almost as soft as lead. It has a specific gravity of about 19.32 (20° C.), melts at 1063° C., and boils at about 2600° C. Native gold has been found crystallized in the cubic system, the octahedron being the most common form.

**Chemical Properties.**--Gold is one of the most inactive and permanent of the metals. Air, oxygen, water, or hydrogen sulfide do not affect it at any temperature. Selenic acid reacts with gold to form auric selenate [Au<sub>2</sub>(SeO<sub>4</sub>)<sub>3</sub>], and is the only single acid that dissolves it. It unites directly with chlorine and bromine, but not with sulfur. It dissolves easily in acid solutions containing free chlorine, bromine or iodine (slowly). Thus, a mixture of nitric and hydro-

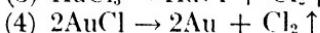
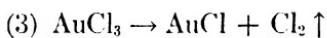
chloric acids (aqua regia), containing free chlorine, nitrosyl chloride and water, dissolves gold with formation of chlorauric acid (1).



Although aqua regia is the best reagent for dissolving gold, the metal can also be dissolved by bromine or chlorine water (2) to form the corresponding gold trihalide.

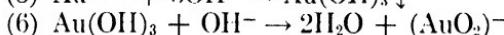


Gold forms two series of salts, the aurous ( $\text{Au}^+$ ) and auric ( $\text{Au}^{+++}$ ), all members of which are quite unstable in that they revert to gold upon sufficient heating. Auric chloride ( $\text{AuCl}_3$ ), for example, is easily converted to aurous chloride ( $\text{AuCl}$ ) by gentle heating (3) and upon stronger heating the aurous chloride is converted to metallic gold (4).

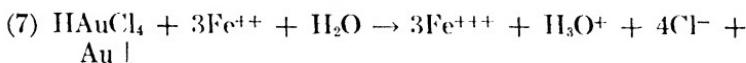


The reactions of the auric series are the most important and will be discussed briefly.

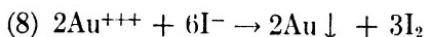
Upon the addition of alkali hydroxides, *e. g.*, sodium hydroxide, there develops a brown precipitate which is soluble in an excess of the reagent. The brown precipitate is auric hydroxide (5), and is easily converted to the aurate (6) with excess alkali. In fact, it is sometimes difficult, especially in dilute gold solutions, to obtain the brown precipitate because of the rapid formation of the aurate.



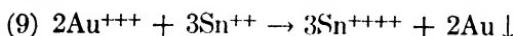
It is important to note that auric compounds are strong oxidizing agents and many of their reactions can be attributed to this property. For example, ferrous salts are readily oxidized to the ferric form with deposition of metallic gold (7).



Addition of potassium iodide to gold solutions results in the formation of metallic gold together with iodine (8).



The reaction of gold with stannous chloride is important. In a highly acidic solution stannous chloride precipitates metallic gold (9), but in a weakly acid or dilute neutral solution the stannous chloride slowly throws down a purple precipitate which is known as the *purple of Cassius*. The reaction is widely used to identify gold. The precipitate is said to consist of colloidal gold and tin hydroxide.

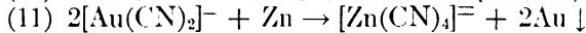
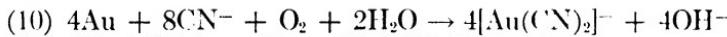


**Official Tests for Gold Ion.**—1. With sodium hydroxide T.S., solutions of auric salts give a brown precipitate (5), which is soluble in an excess of the reagent (6).

2. When treated with stannous chloride T.S., solutions of gold salts slowly form a purple precipitate (purple of Cassius).

**Commercial Manufacture.**—1. Gold is obtained from its alluvial or "placer" deposits by a method that is based on the disintegration of the earthy matter by the action of a stream of water, which washes away the lighter rock (specific gravity about 2.5) and leaves the heavier gold (specific gravity 19.32) in the bottom of a pan, cradle or sluice.

2. The method of mining auriferous quartz rock is about the same as that used for similar deposits of other metals. First, the ore is pulverized in stamping or ball mills and then separated by means of the flotation process or by washing the pulverized material over copper plates amalgamated with mercury. The latter unites with a little over half of the gold to form an amalgam which is then scraped off the plates and separated into gold and mercury by distillation. The "tailings" that run off the separator are treated with a dilute solution of sodium cyanide and the mixture exposed to the air to permit of the formation of soluble sodium aurocyanide (10). Gold is obtained from the solution by electrolysis or by displacement with metallic zinc (11).



Pyrites, containing gold, is usually roasted and then treated with chlorine water (see p. 306), which converts the gold into auric chloride. This is leached out with water and the metal precipitated with ferrous sulfate (see p. 306).

**Pharmacological Action of the Gold Ion.**—A discussion of the pharmacology and therapeutic applications of gold may advantageously be prefaced by a brief historical introduction.

The early use of gold in medicine was of an empirical nature, based largely on legend and folklore. The discovery by Koch in 1890, that gold cyanide was effective *in vitro* against the tubercle bacillus may be said to mark the beginning of modern gold therapy. This discovery led investigators to use various gold salts (less toxic, however, than gold cyanide) in the treatment of many diseases believed to be tuberculous in origin. Its use in the treatment of tuberculosis has been investigated extensively, but the results have been far from satisfying. At present gold is not used in the treatment of this condition. However, from these investigations have stemmed the two principal uses of gold salts today: (1) for lupus erythematosus, and (2) for rheumatoid arthritis.

1. The N. N. R. (1946) said about gold and sodium thiosulfate in the treatment of lupus erythematosus, "A review of the literature in regard to the use of gold and sodium thiosulfate in the treatment of lupus erythematosus reveals, in general, quite satisfactory clinical

results, and it is considered a distinct advance in the therapy of this condition. Although there have been many recurrences in cases originally thought cured, nevertheless the beneficial and often curative action of the drug in a fair percentage of the cases seems to warrant giving it a definite place in the treatment of a disease for which at present there is no specific remedy."

2. The use of gold salts in the treatment of rheumatoid arthritis has been the result of an early belief that this disease was an atypical form of tuberculosis. Although this belief has been dispelled, the sometimes beneficial results of gold therapy in this (the crippling) type of arthritis has led to its retention. Forestier had much to do with the popularization of this form of therapy, and with an increasing appreciation of the toxic possibilities of gold salts the drug is being utilized with less side-effects than previously. The recent literature on the use of BAL (2,3-dimercaptopropanol) in treating the toxic manifestations of gold salts, namely, the gold dermatitides, has been very encouraging and should lead to a more extensive use of gold. However, it is probably advisable to restrict their use to experienced chrysotherapists, and it is well to remember that gold salts probably are not the best answer to the treatment of rheumatoid arthritis.<sup>1</sup>

The soluble gold salts are administered intravenously and most of the drug is excreted in the urine although some is excreted in the feces. Inasmuch as most of the gold is excreted in the urine, it is common to find renal damage as one of the symptoms of gold toxicity. However, the most common difficulty is associated with the skin, the so-called "gold dermatitides."

**Uses.**—Pure gold is too soft for most purposes and, therefore, it is alloyed with copper or silver in order to give it greater hardness. Pure gold is designated as being "24-carat" or 1000 fine. British gold coins (*viz.*, sovereigns) are "22-carat" and hence contain 2 parts of copper and 22 parts of pure gold, equivalent to 91.66 per cent of pure gold, or a fineness of 916.66. United States, French and German gold coins contain 90 per cent of pure gold. Gold, silver and copper alloys (usually 14-carat) are commonly used for making jewelry. Gold is also used for gilding and plating. It is employed in dentistry and for various decorative purposes.

#### OFFICIAL COMPOUNDS OF GOLD

##### GOLD AND SODIUM THIOSULFATE

*Gold and Sodium Thiosulfate*, N. F. VIII

Formula,  $\text{Na}_3\text{Au}(\text{S}_2\text{O}_3)_2 \cdot 2\text{H}_2\text{O}$ . Molecular Weight, 526.47

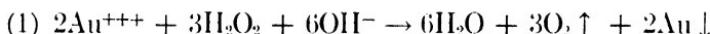
**Physical Properties.**—Gold and Sodium Thiosulfate occurs in white, glistening, needle-like or prismatic crystals. It darkens slowly on exposure to air.

<sup>1</sup> New Eng. J. Med., 235, 362 (1946).

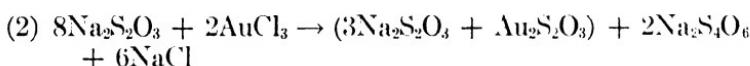
One Gm. of Gold and Sodium Thiosulfate dissolves in 2 cc. of water; it is insoluble in alcohol and most other organic solvents.

**Chemical Properties.**—Aqueous solutions of the salt are neutral or alkaline to litmus paper. The compound, a double salt composed of 3 molecules of sodium thiosulfate ( $\text{Na}_2\text{S}_2\text{O}_3$ ) and 1 molecule of gold thiosulfate ( $\text{Au}_2\text{S}_2\text{O}_3$ ), gives the characteristic reactions of the thiosulfate ion, *e. g.*, decolorization of iodine, precipitation with hot hydrochloric acid, etc. (see also Sodium Thiosulfate, p. 216). It also gives reactions for aurous gold rather than auric.

**Official Tests for Identity.**—1. Fifty mg. of the salt is dissolved in 1 cc. of water in a test-tube. To this is added 1 cc. of diluted hydrochloric acid and the mixture heated on a water-bath causing the evolution of sulfur dioxide and the formation of a brown precipitate of gold sulfide ( $\text{Au}_2\text{S}$ ). The precipitate is washed well with hot water by decantation and then transferred to a porcelain crucible. It is then treated with 3 cc. of hydrochloric acid and 1 cc. of nitric acid to dissolve it and evaporated almost to dryness on a water-bath. To 2 cc. of the filtrate, previously diluted with 5 cc. of water, are added 2 cc. of sodium hydroxide T.S. and 1 cc. of hydrogen peroxide T.S. and the mixture heated on a water-bath. This reaction deposits the gold as a finely divided metal (1) having a purple-red to brownish color. A portion of the filtrate when tested with a few drops of stannous chloride T.S. gives the characteristic purple color.



**Commercial Manufacture.**—Gold and Sodium Thiosulfate is a complex and is probably formed according to the following reaction (2).<sup>1</sup> Although auric chloride is usually used as a starting material, at least one firm uses gold and sodium chloride instead of gold chloride. The gold and sodium thiosulfate which forms in the reaction mixture is precipitated and freed of the other products by the addition of alcohol. No matter what method of preparation is utilized, the gold is reduced from the auric to the aurous state.



**Pharmaceutical Preparations and Uses.**—1. *Gold and Sodium Thiosulfate* (Auri et Sodii Thiosulfas), N. F. VIII. “Gold and Sodium Thiosulfate contains not less than 36.7 per cent and not more than 37.7 per cent of Au.” It is used intravenously for the treatment of lupus erythematosus and rheumatoid arthritis. Average dose—To be determined by the prescriber.

#### NON-OFFICIAL GOLD COMPOUNDS

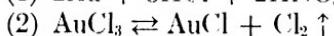
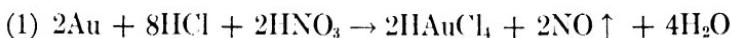
Gold forms an aurous and an auric series of compounds, in which the element is univalent and trivalent, respectively. As has been

<sup>1</sup> Private communication from G. D. Searle & Co., Chicago, Ill., May 13 (1947)

pointed out, all of the compounds of gold are very easily reduced to the metal by heating.

**Oxides.**—Two unstable oxides of gold are known. Aurous oxide ( $\text{Au}_2\text{O}$ ), a violet colored powder, is feebly basic, whereas auric oxide ( $\text{Au}_2\text{O}_3$ ), a brown powder, is amphoteric, but mainly acid-forming. It will be recalled that an amphoteric (or amphiprotic) compound is one that possesses the property of acting either as an acid by losing a proton or as a base by gaining a proton. At  $205^\circ \text{ C.}$  aurous oxide is decomposed. At  $160^\circ \text{ C.}$  auric oxide loses 1 atom of oxygen to form  $\text{Au}_2\text{O}_2$ , which in turn is converted into its elements at  $180^\circ \text{ C.}$

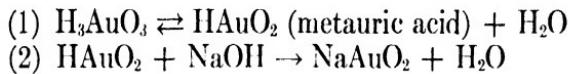
**Halogen Compounds.—Chlorauric Acid and the Chlorides.**—When gold is treated with a mixture of nitric and hydrochloric acids, chlorauric acid is formed (1). When the solution is concentrated, glistening, golden-yellow, deliquescent crystals having the composition  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ , are deposited. Solutions of chlorauric acid may be neutralized with sodium hydroxide to form orange-yellow, rhombic plates or prisms of sodium chloraurate ( $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O}$ ), which is used in photography. This product in no way resembles the *Auri et Sodii Chloridum*, U. S. P. IX, as the latter is a mechanical mixture of equal parts of anhydrous sodium chloride and anhydrouse gold trichloride. Sodium chloraurate ( $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O}$ ) contains 49.5 per cent of gold, whereas the preparation that was formerly official contained only 32 per cent of the metal. Gentle heat decomposes chlorauric acid into red, crystalline auric chlorids ( $\text{AuCl}_3$ ) and hydrogen chloride. When heated to  $180^\circ \text{ C.}$ , auric chloride changes to a yellowish-white powder of aurous chloride and chlorine is evolved (2). Aurous chloride is insoluble in water. Hot water, however, quickly decomposes it into auric chloride and the metal (3).



**Bromauric Acid.**—When gold is treated with bromine water and the resulting solution concentrated, dark, reddish-brown, flat, needle shaped crystals of bromauric acid ( $\text{HAuBr}_4 \cdot 5\text{H}_2\text{O}$ ) separate out. The crystals are odorless and have an acid metallic taste. When pure, the acid is permanent in air. The crystals melt at  $27^\circ \text{ C.}$ , and are very soluble in water and in alcohol.

**Auric Hydroxide and Aurates.**—Caustic alkalies precipitate auric hydroxide ( $\text{Au(OH)}_3$ ) from chlorauric acid or sodium chloraurate. When freshly prepared, it is a yellowish-brown precipitate, which becomes a brown powder on drying. Auric hydroxide is another amphoteric compound having feeble acidic properties. It, there-

fore, interacts with an excess of bases to form aurates (*e. g.*,  $\text{NaAuO}_3 \cdot 3\text{H}_2\text{O}$ ) which are salts of metauric acid (1 and 2).



**Auro and Auri Cyanides.**—The addition of an excess of a solution of a cyanide, *e. g.*,  $\text{NaCN}$ , to aurous and auric salts, respectively, forms colorless and soluble aurocyanides ( $\text{NaAu}(\text{CN})_2$ ) and auri-cyanides ( $\text{NaAu}(\text{CN})_4$ ). These solutions are used as electrolytes in the gold plating of jewelry, ornaments, etc.

## THE ALKALINE EARTH METALS

**Introduction.**--Calcium, strontium and barium are known as the alkaline earth metals. These elements, together with radium, form Division A of Group II in the periodic table. Despite the fact that radium possesses chemical properties that are very similar to those of calcium, strontium and barium, it is usually discussed with the other elements (Rn, Ac, Th, Pa, U) having the unusual property of radioactivity. The electropositivity of the members of this family is surpassed only by that of the alkali metals. Like the latter, the activity increases as the atomic weights increase.

These elements are bivalent and never react to form complex ions. They all act energetically on water, liberating hydrogen and forming hydroxides. The elements unite directly with hydrogen and nitrogen to form the respective hydrides ( $XH_2$ ) and nitrides ( $X_3N_2$ ). The oxides of these metals are formed by heating the hydroxides, carbonates or nitrates. They are infusible at high temperatures and are not reduced by hydrogen or carbon under such conditions. The hydroxides of this group are not as soluble in water as those of the alkalies but, nevertheless, they resemble them by being active bases. On the other hand, the carbonates, sulfates, phosphates and fluorides, unlike the corresponding salts of the alkalies, are almost insoluble in water. From a standpoint of stability, the compounds of the elements of this family are between those of the alkalies and those of the heavy metals. Their stability increases as the atomic weights of the elements increase. Thus, calcium (atomic weight, 40.08) compounds are the easiest to decompose, whereas those of barium (137.36) are the most difficult. The alkaline earth metals never occur free in Nature. In combination, chiefly as carbonates and sulfates, they are widely and abundantly distributed.

## CHAPTER XVIII

### CALCIUM AND CALCIUM COMPOUNDS

#### CALCIUM

Symbol, Ca. Valence, II. Atomic Weight, 40.08;  
Atomic Number, 20

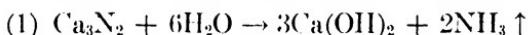
**History.**--A description of the process of calcining limestone (lime burning) is found in the writings of Dioscorides and Pliny. The ancients used lime in mortar for building purposes. In 1808, Davy obtained the first calcium metal by electrolysis.

**Occurrence.**—Calcium is never found free in Nature. In combination it is widely distributed and occurs most abundantly in the form of the carbonate. This is found in a comparatively pure condition as *chalk*, *marble*, *limestone*, *calcite*, *aragonite*, and *marl*. Many other minerals, notably *dolomite*, contain the carbonate as one of the constituents. Calcium also occurs in large quantities as *fluorspar* or *fluorite* [CaF<sub>2</sub>], *gypsum* or *seLENite* [CaSO<sub>4</sub>.2H<sub>2</sub>O], *anhydrite* [CaSO<sub>4</sub>], *phosphate rock* [Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>], and as a constituent of nearly all silicates. Both plants and animals contain calcium in some combined form.

**Physical Properties.**—Calcium is a silvery-white, crystalline (cubic) metal, which gradually becomes gray by oxidation. It is harder than lead and may be cut, drawn, and rolled. It has a density of 1.54 melts at 810° C., and boils at 1240° C.

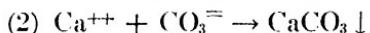
**Chemical Properties.**—The chemical properties of calcium will be considered under the headings: (1) metallic calcium, and (2) the calcium ion.

1. Calcium readily decomposes water at ordinary temperatures with the rapid evolution of hydrogen. The heat developed by this reaction is insufficient to inflame the latter (difference from alkali metals). Oxygen, hydrogen, nitrogen, sulfur, phosphorus, and the halogens do not readily attack the metal in the cold. However, when it is heated they combine vigorously with it. Calcium burns in air with a brilliant white flame to form calcium oxide (CaO) and calcium nitride (Ca<sub>3</sub>N<sub>2</sub>). The latter is acted upon by water and forms ammonia and the hydroxide of the metal (1).



Calcium forms an amalgam with mercury.

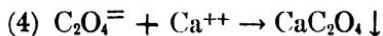
2. The chief chemical reactions involving the calcium ion are those of precipitation, because, as indicated in the introduction, the alkaline earth metals form many insoluble salts. A typical example is that of the carbonate ion which readily precipitates calcium as the insoluble carbonate (2).



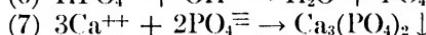
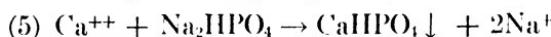
This reaction is involved in the testing of solutions for calcium, *i. e.*, by passing CO<sub>2</sub> into a solution of calcium hydroxide. It is interesting to note that even though insoluble calcium carbonate does form, it is possible to solubilize it by passing into the cold solution more CO<sub>2</sub> (3) to form soluble calcium bicarbonate.



Soluble oxalate salts also precipitate calcium as insoluble calcium oxalate (4). This reaction was the basis of the poisonous action of the ill-famed "Elixir of Sulfanilamide" in which the solvent was ethylene glycol. This was readily oxidized in the body to oxalic acid which in turn precipitated the calcium in the blood as insoluble calcium oxalate.



When neutral solutions of calcium salts are treated with soluble phosphates such as sodium phosphate, a white, flocculent precipitate of insoluble secondary calcium phosphate forms (5). If, however, the solution is made ammoniacal, the precipitate which forms is tertiary calcium phosphate (6, 7).



Calcium ion is also precipitated by sulfate ions as more or less insoluble calcium sulfate (8), but it requires a fairly high concentration of sulfate ion because calcium sulfate is appreciably soluble.



Volatile compounds of calcium impart a reddish-yellow color to a non-luminous flame, and non-volatile calcium salts will do the same when moistened with hydrochloric acid.

Many of the calcium salts exhibit a peculiar solubility in that they are more soluble in cold solutions than they are in hot solutions.

**Official Tests for Identity.**—1. In neutral or alkaline solutions calcium salts produce a white precipitate when treated with ammonium oxalate T.S. (4). The precipitate is insoluble in acetic acid but is soluble in hydrochloric acid.

2. Calcium salts when moistened with hydrochloric acid will impart a transient yellowish-red color to a non-luminous flame.

**Commercial Manufacture.**—Calcium is made by the electrolysis of the molten chloride. The process is carried out in a crucible made of iron and lined with blocks of graphite securely fastened together. This acts as the anode. A rod of iron serves as the cathode. The crucible is filled with anhydrous calcium chloride, which is melted by temporarily connecting the anode and cathode with a thin rod of carbon. As soon as fusion has begun, the carbon rod is removed. The resistance of the fused material is sufficient to maintain the temperature. The calcium is liberated at the end of the cathode and collects upon the surface of the melt. When the cathode is drawn slowly from the bath, the calcium, which adheres to it, is obtained in the form of an irregular rod. At no time during the run is the calcium rod separated from the molten metal cathode on the surface of the bath, as this would cut off the current and the reaction would cease.

The metal is sometimes used instead of Na or K as a reducing agent in organic synthesis and for dehydrating oils, etc.

**Pharmacological Action of the Calcium Ion.**—Calcium is extremely important in the maintenance of certain normal body functions. It is important in the following capacities:

1. As an indispensable cation relating to the functional integrity of the voluntary and autonomic nervous systems.
2. As a factor in proper cardiac function.
3. As a factor in blood coagulation.
4. As the structural basis of the skeleton and like tissue.

Ordinarily, sufficient calcium is ingested in the normal diet (0.45 Gm. daily requirement) to supply the body needs. The ingested calcium is absorbed in the upper portion of the intestinal tract and is excreted in the urine and feces. An acid condition in the intestine favors absorption of calcium salts because of better solubility in the acid medium. An alkaline reaction retards absorption by favoring precipitation of insoluble calcium salts. Likewise, a high fatty acid content in the bowel slows down absorption by forming insoluble calcium soaps.

The calcium of the body exists principally in the form of the bony skeleton as calcium carbonate and phosphate. The rest of the calcium is found in the extracellular fluid (see p. 147) in the form of soluble simple salts, combinations with serum protein (as undissociated calcium), and soluble calcium complexes. There is a balance in the body between the various forms of calcium, but the ionic form of calcium is the only one which is physiologically active.

Reduction in the amount of ionized calcium in the blood causes a hypocalcemic tetany characterized by an increased irritability of all types of nerve and muscle. On the other hand, serum calcium in excess has the opposite effect and from the pharmacological point of view may be considered as a nerve sedative.

Calcium has a cardiac action similar to digitalis, and it is believed that high calcium concentrations increase the toxicity of digitalis. The cardiac effects of calcium are related to the delicate balance between calcium and potassium ion, either one when in excess causing cessation of heart beat. Excess potassium causes a diastolic arrest, whereas excess calcium causes systolic arrest.

It is believed by some that calcium decreases the permeability of the capillaries and thereby prevents edemas, etc. This belief has not been well received and consequently calcium is little used for this purpose.

The rôle of calcium in blood clotting is well known and does not require further elaboration. However, it is well to point out that calcium deficiency rarely, if ever, is the cause of prolonged blood clotting time. Increasing calcium intake never shortens the clotting time.

Nutritional deficiencies of calcium lead to faulty growth. The need for calcium therapy in these conditions may result from insufficient intake, insufficient vitamin D, etc. Vitamin D is essential for the maximum absorption of dietary calcium and this fact is reflected in the many calcium preparations on the market to which vitamin D has been added. Insufficient calcium in the diet tied together with too little calcium in the skeleton results in rickets in children and osteomalacia in adults.

A more or less new use of calcium salts is in the control or relief of various allergic manifestations, *i. e.*, eczema, pruritus and urticaria. On the theory that these allergies are exhibitions of vagotonia (irritability of the vagus nerve) and because calcium and magnesium are nerve sedatives, it would logically follow that

intensive calcium therapy would relieve such conditions. This has proven correct and therefore calcium is much used intravenously in combination with bromine (as calcium bromide or organic calcium bromide combinations) to decrease skin sensitivity in the aforementioned diseases. The accompanying diagram (Fig. 14) shows the recognized and experimental indications for calcium therapy.

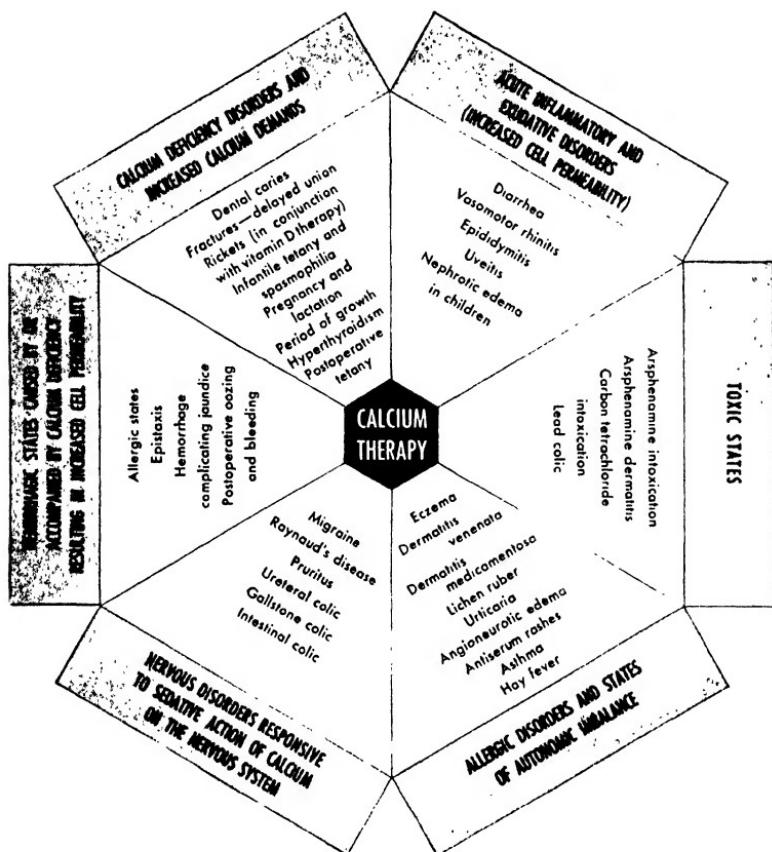


FIG. 14.- Recognized and experimental indications for calcium therapy. (Roche Review, June-July, 1944. Permission to reproduce granted by the editors, Hoffmann La Roche, Inc., Nutley, N. J.)

Calcium salts are also used as acid-forming diuretics, the mechanism of action in the case of calcium chloride being analogous to that of ammonium chloride. However, the calcium ion is removed from the chloride as insoluble calcium phosphate, whereas ammonium ion is disposed of as urea (see p. 264).

Some of the insoluble calcium salts, *e. g.*, calcium carbonate, are used as gastric antacids. It is claimed that salts of this type are less apt to cause a systemic alkalosis than are soluble antacids such as sodium bicarbonate.

## OFFICIAL CALCIUM COMPOUNDS

## CALCIUM BROMIDE

*Calcium Bromide*, N. F. VIIIFormula,  $\text{CaBr}_2$ . Molecular Weight, 199.91

**Physical Properties.**—Calcium Bromide is a white, granular salt. It is odorless and has a bitter taste. It is very deliquescent.

One Gm. of the salt dissolves in about 0.7 cc. of water and in about 1.3 cc. of alcohol, at  $25^\circ \text{ C}$ . One Gm. is soluble in about 0.4 cc. of boiling water. It is insoluble in chloroform and in ether.

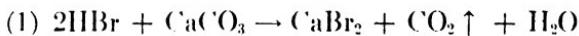
When heated at red heat, the salt fuses and gives off vapors of bromine. Anhydrous calcium bromide ( $\text{CaBr}_2$ ) melts at  $765^\circ \text{ C}$ .; the trihydrate ( $\text{CaBr}_2 \cdot 3\text{H}_2\text{O}$ ) at  $80.5^\circ \text{ C}$ ., and the hexahydrate ( $\text{CaBr}_2 \cdot 6\text{H}_2\text{O}$ ) at  $38.2^\circ \text{ C}$ .

**Chemical Properties.**—Aqueous solutions of calcium bromide give the reactions characteristic of calcium ion (*q. v.*) and bromide ion (*q. v.*).

**Official Tests for Identity.**—1. A solution (1 in 20) of Calcium Bromide in water gives the tests for *Calcium* (*q. v.*).

2. A solution also gives the tests for *Bromide* (*q. v.*).

**Commercial Manufacture.**—Calcium bromide is usually prepared by adding precipitated calcium carbonate to dilute hydrobromic acid until effervescence ceases (1). The neutral solution is filtered to remove excess of calcium carbonate and then evaporated to dryness.



**Pharmaceutical Preparations and Uses.**—1. *Calcium Bromide* (Calcii Bromidum), N. F. VIII.—“Calcium Bromide is a hydrated salt, containing not less than 84 per cent and not more than 94 per cent of  $\text{CaBr}_2$ .” The usual chemical formula assigned to this salt is  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$ . Calcium bromide is usually used for the same purposes as any other bromide salt, namely for the sedative action of the bromide ion. However, as previously indicated, calcium bromide may be used to take advantage of the synergistic action of calcium and bromine, since both are nerve sedatives. However, calcium bromide is unsatisfactory because of its unpalatability, irritant action, etc. If administered parenterally, it should only be given intravenously and then in dilute solutions. Another disadvantage claimed for calcium bromide is that the ratio of bromine to calcium is too high, it being 4 to 1. In an effort to overcome these difficulties workers have turned to organic combinations with calcium bromide. One of such products is calcium galactogluconate-calcium bromide which has a bromine to calcium ratio of 2 to 1 and is much more pleasant to use. It is much more satisfactory for intravenous use and has advantages in the treatment of the various allergic

diseases previously mentioned. Average dose—1 Gm. (approximately 15 grains).

2. *Five Bromides Elixir* (*Elixir Bromidorum Quinque*), N. F. VIII.—Contains 5.2 per cent of calcium bromide together with varying quantities of other bromides. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Bromides Syrup* (*Syrupus Bromidorum*), N. F. VIII.—This syrup contains 2.5 per cent of calcium bromide together with varying quantities of other bromides. Average dose—4 cc. (approximately 1 fluidrachm).

### CALCIUM CARBONATE

*Precipitated Calcium Carbonate*, U. S. P. XIII

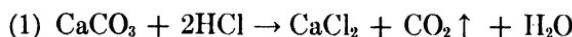
Formula,  $\text{CaCO}_3$ . Molecular Weight, 100.09

**Occurrence.**—Calcium carbonate is the most abundant and widely distributed calcium salt. It occurs as chalk, limestone, marble, aragonite and calcite, and is one of the chief constituents of shells (eggs and mollusks), corals and pearls. (See Calcium, p. 313.) In chalk it is amorphous, in limestone it is in a massive, indistinctly crystalline form, in marble it is crystalline, whereas in calcite and aragonite it occurs as distinct crystals. The dimorphic character of calcium carbonate is illustrated by the last two forms. When carbon dioxide is passed into cold lime water, or when a cold aqueous solution of a calcium salt is treated with a solution of a carbonate, a flocculent, amorphous precipitate is produced, which soon becomes crystalline (calcite). Calcite is more abundant than aragonite in Nature and occurs as hexagonal crystals having a specific gravity of 2.711 at  $25.2^\circ \text{ C}$ . On the other hand, if hot solutions of the reacting substances are mixed, a crystalline precipitate is formed immediately (aragonite). Aragonite occurs in Nature as rhombic prisms having a specific gravity of 2.93 at  $40^\circ \text{ C}$ .

**Physical Properties.**—Precipitated Calcium Carbonate is a fine, white microcrystalline powder. It is odorless and tasteless. It is stable in air.

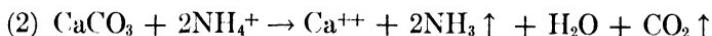
The salt is nearly insoluble in water (0.065 Gm. per liter at  $20^\circ \text{ C}$ ). The water solubility is increased by the presence of  $\text{CO}_2$  (see p. 313) and also by ammonium salts (except ammonium carbonate). The water solubility is decreased in the presence of alkali hydroxides. It is insoluble in alcohol, but is soluble in most acids with effervescence.

**Chemical Properties.**—One of the principal chemical properties of calcium carbonate, of course, is its ability to neutralize acids. This is a common property of all other carbonates. A typical example is the reaction with hydrochloric acid (1).

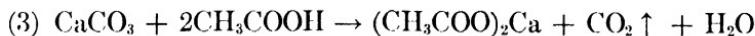


The solubility of calcium carbonate in ammonium salts is accounted for in the following equation (2). The reaction does not go to

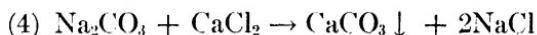
completion unless the mixture is boiled with a large excess of the ammonium salt.



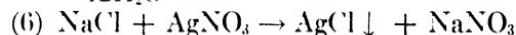
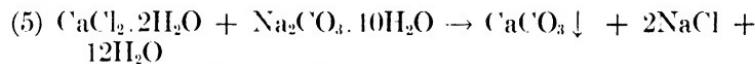
**Official Tests for Identity.**—1. The addition of acetic acid to calcium carbonate produces an effervescence (3), and the resulting solution, after boiling to expel carbon dioxide and neutralizing the excess acid, responds to all tests for the calcium ion (*q. v.*).



**Commercial Manufacture.**—Calcium carbonate is prepared commercially by the interaction of sodium carbonate and calcium chloride (4). It is prepared in various grades for widely different uses.



**Laboratory Preparation.**—Dissolve 26 Gm. of sodium carbonate ( $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$ ) and 13.4 Gm. of calcium chloride ( $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ ) each in 100 cc. of distilled water and filter the solutions. Warm both of the solutions to about  $60^\circ \text{C}$ . and pour the calcium chloride solution into the solution of sodium carbonate, constantly stirring the mixture (5). Wash the precipitate on a filter with warm water until a portion of the filtrate, when acidified with diluted nitric acid, does not give a precipitate with silver nitrate test solution (6). Wash the precipitate of calcium carbonate, dry it in an oven, and powder.



When calcium carbonate is precipitated in the cold, it is at first flocculent and quite voluminous, but slowly changes to a very fine micro-crystalline product, which is more difficult to wash free from chlorides than when precipitated from warm solutions. (See specific gravity of calcium carbonate, p. 318.)

**Pharmaceutical Preparations and Uses.**—1. *Precipitated Calcium Carbonate* (*Calcii Carbonas Praecipitatus*, Precipitated Chalk), U. S. P. XIII.—“Precipitated Calcium Carbonate, when dried at  $200^\circ$  for 4 hours, contains not less than 98.5 per cent of  $\text{CaCO}_3$ .” This preparation is used *externally* as a dentifrice because it has a mild abrasive quality due to its microcrystalline structure. It is used internally as an antacid because of its acid neutralizing powers. As previously pointed out (see p. 316), its water insolubility makes it less apt to cause systemic alkalosis. Some investigators<sup>1</sup> have been able, however, to show that calcium carbonate is capable of producing alkalosis in spite of its water-insolubility and, furthermore, that calcium carbonate has a tendency to cause constipation.

<sup>1</sup> Kirsner and Palmer; J. Am. Med. Assn., 116, 384 (1941).

Calcium carbonate in other grades than the pharmaceutical grade is used for a variety of purposes. Many fine baking powders contain this chemical, and the coated paper of quality magazines owes its whiteness and brightness to calcium carbonate. This versatile chemical is an excellent reinforcing agent for rubber, lending tensile strength and tear resistance to hot-water bottles, rubber gloves, auto tubes, etc.

Calcium carbonate in the form of limestone and marble has long been used as a building material. Limestone is also used for making lime, calcium carbide, calcium cyanide, glass, and in metallurgy (especially as a flux in smelting iron ores).

Chalk occurs widely distributed, and is found abundantly on the coast of the English Channel. It is composed of minute shells of marine animals (*Foraminifera*), and besides calcium carbonate, contains small amounts of silica, iron, aluminum, magnesium and organic matter. A chalk, especially prepared for internal use, is used as an antacid (see p. 321). Average dose—1 Gm. (approximately 15 grains).

2. *Penicillin Tablets* (Tabellæ Penicillini), U. S. P. XIII.—(See also p. 184.) Calcium carbonate may be used in these tablets to act as a buffer in the gastric juices, thus preventing excessive destruction of the penicillin in the stomach. Average daily dose of penicillin—On a fasting stomach, 300,000 units.

3. *Calcium Carbonate Tablets* (Tabellæ Calcii Carbonatis), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{CaCO}_3$ ." Like the powder, the tablets are used as an antacid.

4. *N. F. Dentifrice* (Dentifricium N. F., N. F. Tooth Powder), N. F. VIII.—N. F. Dentifrice contains 93.5 per cent of precipitated calcium carbonate together with 5 per cent of hard soap and small quantities of flavoring agents. The precipitated calcium carbonate provides the abrasive qualities for this efficient dentifrice.

5. *Sodium Bicarbonate and Calcium Carbonate Powder* (Pulvis Soda Bicarbonatis et Calcii Carbonatis, Sippy Powder No. 1), N. F. VIII.—(See p. 158.) This preparation makes use of the antacid action of calcium carbonate and contains 23 per cent of precipitated calcium carbonate, together with 77 per cent of sodium bicarbonate. Average dose—2.6 Gm. (approximately 40 grains).

6. *Sodium Bicarbonate and Calcium Carbonate Tablets* (Tabellæ Soda Bicarbonatis et Calcii Carbonatis, Sippy Powder Tablets No. 1), N. F. VIII.—This preparation contains Sippy powder in tablet form for convenient administration.

7. *Compound Sulfur Ointment* (Unguentum Sulfuris Compositum, Wilkinson's Ointment, Hebra's Itch Ointment), N. F. VIII.—This ointment contains 10 per cent of precipitated calcium carbonate together with sublimed sulfur and juniper tar (15 per cent each), and soft soap and solid petroxolin (30 per cent each). The calcium carbonate is said to be present for the purpose of combining with thiolic and thionic acids which are formed when sulfur is in con-

tact with the skin. The resulting calcium salts then exert an active parasiticidal action. This ointment is much used in the treatment of scabies (itch), but it has been superseded by better agents (see p. 564).

8. *Zinc Oxide Soft Paste* (*Pasta Zinci Oxidi Mollis*, Unna's Soft Zinc Paste), N. F. VIII.—This preparation contains 25 per cent each of zinc oxide and precipitated calcium carbonate, together with appropriate quantities of oleic acid, linseed oil and calcium hydroxide solution. When applied to the skin this paste acts as a drying paste with a mild antiseptic and astringent action.

**Prepared Chalk** (*Creta Praeparata*, Drop Chalk), U. S. P. XIII.—Prepared chalk is a native form of calcium carbonate that has been freed from most of its impurities by elutriation. It contains, when dried to constant weight at 200° C., not less than 97 per cent of  $\text{CaCO}_3$ .

It is a white to grayish-white, microcrystalline powder. It is often prepared in cones, sometimes called "conical drops." It is odorless, tasteless, and stable in the air. Prepared chalk responds to all the tests for identity given under calcium carbonate (*q. v.*).

Prepared chalk is made by the process of elutriation. This consists in suspending the powdered native chalk in cold water, allowing the heavier materials to subside and straining the milky aqueous suspension of the finer particles through suitable cloths. The pasty mass is transferred from the strainer to a funnel, from which it is dropped upon porous tiles. The more or less coarse material that settles out is known as "whiting."

Prepared chalk is to be preferred to precipitated calcium carbonate for internal administration because it is more impalpable and because it possesses marked adhesive properties. It is an excellent antacid and, on account of its mild, non-irritating protective action, is employed in the treatment of various forms of diarrhea. It is possible that the depressant calcium-ion action contributes to its efficacy. Average dose—1 Gm. (approximately 15 grains).

It is an important constituent of the following preparations:

1. *Chalk Mixture* (*Mistura Cretæ*), U. S. P. XIII.—This preparation contains 6 per cent of prepared chalk held in suspension by bentonite magma and flavored with saccharin sodium and cinnamon water. Average dose—15 cc. (approximately 4 fluidrachms).

2. *Aromatic Chalk Powder* (*Pulvis Cretæ Aromaticus*), N. F. VIII.—This preparation contains 25 per cent of prepared chalk together with sucrose and flavoring agents. Average dose—2 Gm. (approximately 30 grains).

3. *Compound Chalk Powder* (*Pulvis Cretæ Compositus*), N. F. VIII.—This preparation contains 30 per cent of prepared chalk, 20 per cent of acacia and 50 per cent of sucrose. Average dose—2 Gm. (approximately 30 grains).

4. *Mercury With Chalk* (*Hydrargyrum cum Creta*), N. F. VIII.—"Mercury with Chalk contains not less than 36 per cent and not more than 40 per cent of Hg." In addition to mercury it contains

57 per cent of prepared chalk, 10 per cent of honey and the remainder distilled water. It is used as a mild mercurial laxative. Average dose—0.25 Gm. (approximately 4 grains).

### CALCIUM CHLORIDE

*Calcium Chloride*, U. S. P. XIII

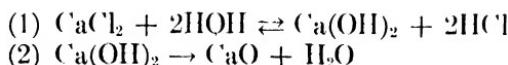
Formula,  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ . Molecular Weight, 147.03

**Occurrence.**—Calcium chloride occurs as *tachhydrite* ( $\text{CaCl}_2 \cdot 2\text{MgCl}_2 \cdot 12\text{H}_2\text{O}$ ) at Stassfurt. It is found in some other minerals, in sea water and in many mineral waters. In the fourteenth century, Isaac Hollendus prepared it by heating a mixture of lime and sal ammoniac.

**Physical Properties.**—Calcium Chloride occurs as white, hard fragments or granules. It is odorless and has a sharp, bitter, saline taste. It is very deliquescent.

One Gm. of Calcium Chloride dissolves in 1.2 cc. of water and in about 10 cc. of alcohol, at  $25^\circ \text{ C}$ . One Gm. also dissolves in 0.7 cc. of boiling water and in about 2 cc. of boiling alcohol. It is insoluble in ether, chloroform, and in fixed and volatile oils. Because of its great solubility in water, the salt forms an excellent freezing mixture with ice. When 1 part of the salt is mixed with two-thirds of its weight of crushed ice it gives a temperature of  $-45^\circ \text{ C}$ .

**Chemical Properties.**—Calcium chloride forms several hydrates, *viz.*, the monohydrate,  $\text{CaCl}_2 \cdot \text{H}_2\text{O}$ , the dihydrate,  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ , the tetrahydrate,  $\text{CaCl}_2 \cdot 4\text{H}_2\text{O}$ , and the hexahydrate,  $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$ . When aqueous solutions of the salt are evaporated, there are obtained large, hexagonal prisms of the hexahydrate, which melt at  $29.92^\circ \text{ C}$ . and have a specific gravity of 1.6817 at  $\frac{2}{3}^\circ \text{ C}$ . Upon the application of heat, all of the hydrates lose part of their water of hydration and are converted into a porous mass which is used for drying gases and liquids. It should be noted that during the heating, some calcium oxide is formed by the reaction of some of the calcium chloride with water (1) (2).

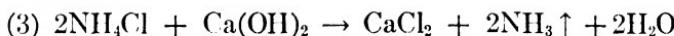


Although anhydrous calcium chloride is widely used for drying organic liquids, gases, etc., it is unsuited as a drying agent for alcohols because it forms crystalline compounds known as *alcoholates* with them:  $\text{CaCl}_2 \cdot 4\text{C}_2\text{H}_5\text{OH}$ ;  $\text{CaCl}_2 \cdot 4\text{CH}_3\text{OH}$ . It is likewise unsuited for drying ammonia gas, since it unites directly with it, forming a compound,  $\text{CaCl}_2 \cdot 4\text{NH}_3$ . The chemical properties of calcium chloride are exhibited by the reactions of the calcium ion and of the chloride ion.

**Official Tests for Identity.**—1. A 1 in 10 aqueous solution of calcium chloride responds to the tests for *Calcium* (*q. v.*).

2. The aqueous solution also responds to the tests for *Chloride* (*q. v.*).

**Commercial Manufacture.**—Calcium chloride is a by-product of many industrial processes of which perhaps the Solvay soda process is the most important. In this process ammonium chloride is a by-product at the time sodium bicarbonate is formed (see p. 170). The sodium bicarbonate is in suspension in the solution containing the ammonium chloride and is then filtered out. The recovery of the ammonia from the ammonium chloride is accomplished by treating this solution with milk of lime,  $\text{Ca}(\text{OH})_2$  (3), leaving calcium chloride as a by-product. The liberated ammonia, of course, is easily obtained from the solution by heating, and the remaining solution needs only to be concentrated to obtain the solid calcium chloride.



**Pharmaceutical Preparations and Uses.**—1. *Calcium Chloride* (Calci Chloridum), U. S. P. XIII.—“Calcium Chloride contains not less than 75 per cent and not more than 81 per cent of  $\text{CaCl}_2$ .” This salt is one of the important calcium salts used in modern therapy. When calcium chloride is administered, the calcium is disposed of by the body as insoluble calcium phosphate and is excreted by way of the bowel. The chloride portion of the molecule acts in a manner similar to hydrochloric acid, *i. e.*, to decrease the alkali reserve of the body. It is for this reason that calcium chloride is often administered to produce an acid urine or a definite acidosis (as in the treatment of calcium tetany). While calcium chloride may be used for the calcium content, and sometimes is, it has never been shown that it is superior to any other calcium salt. In fact, calcium chloride is inferior for oral administration because of its unpleasant taste and highly irritating nature. If it is to be administered orally, however, it should be combined with a demulcent vehicle, such as milk, to minimize the irritation. Likewise, it is not the best preparation for parenteral administration since it cannot be used intramuscularly or subcutaneously due to its irritating and corrosive characteristics. Therefore, its use is confined to intravenous injection. Because of the disadvantages associated with the use of calcium chloride, efforts have been made to modify the calcium chloride molecule in such a way as to minimize the unpleasant side-effects. As a result, a compound chemically named calcium chloride urea,  $\text{CaCl}_2 \cdot 4(\text{NH}_2)_2\text{CO}$ , and commercially named Afenil was made. It is administered intravenously, not orally, and is said to be much better tolerated and less irritating than calcium chloride.

2. *Ringer's Solution* (Liquor Ringeri, Isotonic Solution of Three Chlorides, U. S. P. XII), U. S. P. XIII.—This preparation contains in each 100 cc. not less than 30 mg. and not more than 36 mg. of  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$  together with appropriate quantities of other chlorides (Na and K). (See also p. 178.)

3. *Lactated Ringer's Solution* (Liquor Ringeri Lacticus), U. S. P. XIII.—This solution contains in each 100 cc. not less than 18 mg. and not more than 22 mg. of  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$  together with other chlorides (K and Na) and sodium lactate. (See also p. 178.)

4. *Calcium Chloride Ampuls* (Ampullæ Calcii Chloridi), N. F. VIII.—These ampuls "contain a sterile solution of calcium chloride in water for injection, and yield  $\text{CaCl}_2$ , equal to not less than 72 per cent and not more than 79 per cent of  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ ." This is simply a convenient form of medication for intravenous injection. Average dose—1 Gm. of Calcium Chloride.

5. *Pectin Paste* (Pasta Pectini), N. F. VIII.—The calcium chloride in this preparation is supplied by Ringer's solution. (See also p. 180.)

6. *Thin Pectin Paste* (Pasta Pectini Tenuis), N. F. VIII.—This preparation contains Ringer's solution, of which calcium chloride is an ingredient. (See also p. 180.)

### CALCIUM GLUCONATE

*Calcium Gluconate*, U. S. P. XIII

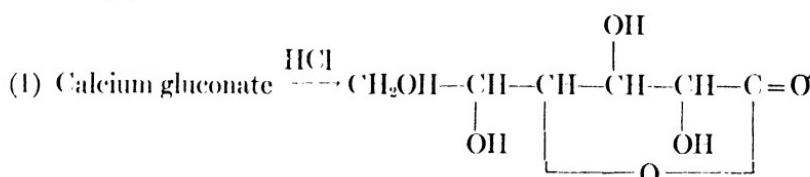
Formula,  $\text{Ca}(\text{C}_6\text{H}_{11}\text{O}_7)_2 \cdot \text{H}_2\text{O}$ ;  $[\text{CH}_2\text{OH}(\text{CHOH})_4 \cdot \text{COO}]_2\text{Ca} \cdot \text{H}_2\text{O}$

Molecular Weight, 448.39

**Physical Properties.**—Calcium Gluconate occurs as a white, crystalline or granular powder without odor or taste. It is stable in air.

One Gm. of Calcium Gluconate dissolves slowly in about 30 cc. of water at  $25^\circ \text{ C.}$ , and in about 5 cc. of boiling water. It is insoluble in alcohol and in other organic solvents.

**Chemical Properties.**—Solutions of calcium gluconate respond to all reactions of the calcium ion. Addition of hydrochloric acid or other acids to solutions of calcium gluconate cause the formation of gluconic acid in solution, although it will not precipitate out. The gluconic acid is said to be converted quite easily to d-glucono-lactone (1).



**Official Tests for Identity.**—1. A 1 in 50 solution of Calcium Gluconate responds to the tests for *Calcium* (*q. v.*).

2. To 5 cc. of a warmed 1 in 10 aqueous solution of Calcium Gluconate is added 0.65 cc. of glacial acetic acid (2) and 1 cc. of freshly distilled phenylhydrazine. The mixture is heated on a water-bath for thirty minutes and allowed to cool. When the solution is cool and particularly when the inside of the tube is scratched with a glass rod, crystals of gluconic-acid-phenylhydrazone form (3).

- (2)  $[\text{CH}_2\text{OH}(\text{CHOH})_4.\text{COO}]_2\text{Ca} \cdot \text{H}_2\text{O} + 2\text{HCl}_2\text{H}_3\text{O}_2 \rightarrow 2\text{CH}_2\text{OH} \cdot (\text{CHOH})_4.\text{COOH} + \text{Ca}(\text{C}_2\text{H}_3\text{O}_2)_2 + \text{H}_2\text{O}$   
 (3)  $\text{CH}_2\text{OH}(\text{CHOH})_4.\text{COOH} + \text{C}_6\text{H}_5\text{NH} \cdot \text{NH}_2 \rightarrow \text{CH}_2\text{OH} \cdot (\text{CHOH})_4\text{CO} \cdot \text{NH} \cdot \text{NH} \cdot \text{C}_6\text{H}_5 \downarrow + \text{H}_2\text{O}$

**Commercial Manufacture.**—Calcium gluconate may be prepared either by the oxidation of glucose to gluconic acid in the presence of calcium carbonate or by first preparing gluconic acid and then adding calcium carbonate to form the salt. In the former method the oxidation of glucose is effected either by bromine or by electrolytic oxidation in the presence of sodium bromide. In the latter procedure, the gluconic acid is usually obtained by the action of various moulds or bacteria of the Acetobacter group upon glucose.

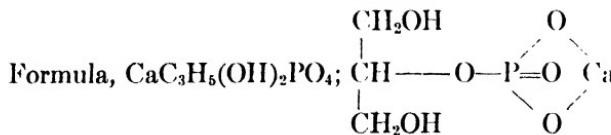
**Pharmaceutical Preparations and Uses.**—1. *Calcium Gluconate* (*Calcii Gluconas*), U. S. P. XIII.—This salt “contains not less than 8.8 per cent and not more than 9.3 per cent of calcium (Ca), corresponding to not less than 99 per cent of  $\text{Ca}(\text{C}_6\text{H}_{11}\text{O}_7)_2 \cdot \text{H}_2\text{O}$ .” It is used as a source of calcium ion both for oral, intravenous and intramuscular use, and is much superior to calcium chloride in that it tastes better and is much less irritating. The salt is used extensively in the treatment of milk fever in cows. Average dose—Oral, 5 Gm. (approximately 75 grains); Intramuscular or intravenous, 1 Gm. (approximately 15 grains).

2. *Calcium Gluconate Injection* (*Injectio Calcii Gluconatis*), U. S. P. XIII.—This injection “is a sterile solution of calcium gluconate in water for injection. It contains not less than 95 per cent and not more than 105 per cent of the labeled amount of  $\text{Ca}(\text{C}_6\text{H}_{11}\text{O}_7)_2 \cdot \text{H}_2\text{O}$ .” It is permissible to add calcium d-saccharate, or other calcium salts as stabilizers provided, however, that the amount of such added calcium salts, calculated as calcium (Ca), does not exceed 5 per cent of the calcium (Ca) present as calcium gluconate. For the purpose of insuring greater stability, it is also permitted to adjust the pH with sodium hydroxide to not above 8.2. Average dose of Calcium Gluconate—Intramuscular or intravenous, 1 Gm. (approximately 15 grains).

3. *Calcium Gluconate Tablets* (*Tabellæ Calcii Gluconatis*), N. F. VIII.—These tablets “contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{Ca}(\text{C}_6\text{H}_{11}\text{O}_7)_2 \cdot \text{H}_2\text{O}$ .” The tablets provide a convenient form for orally administering calcium gluconate. Average dose—5 Gm. (approximately 75 grains) of Calcium Gluconate.

## CALCIUM GLYCEROPHOSPHATE

### *Calcium Glycerophosphate*, N. F. VIII



Molecular Weight 210.15

**Physical Properties.**—Calcium glycerophosphate is a fine, white, odorless and almost tasteless powder. It is slightly hygroscopic.

One Gm. of the salt dissolves in about 50 cc. of water at 25° C. Its solubility in water increases as the temperature decreases. The presence of citric acid increases its solubility in water. It is insoluble in alcohol.

**Chemical Properties.**—When calcium glycerophosphate is heated above 170° C., it is decomposed with the evolution of inflammable vapors. At red heat it is converted to calcium pyrophosphate.

The principal chemical properties of this compound may be attributed to the calcium ion (*q. v.*) and the phosphate ion which result on decomposition of the glycerophosphoric acid. (See Sodium Glycerophosphate, p. 186.)

**Official Tests for Identity.**—1. A saturated solution responds to the tests for *Calcium* (*q. v.*) and *Glycerophosphate* (*q. v.*).

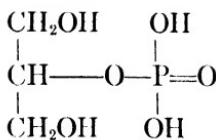
2. When a cold, saturated, aqueous solution of the salt is raised to boiling, small iridescent scales of anhydrous calcium glycerophosphate separate out.

3. When heated strongly it decomposes giving off inflammable vapors, and when heated to red heat, calcium pyrophosphate is formed.

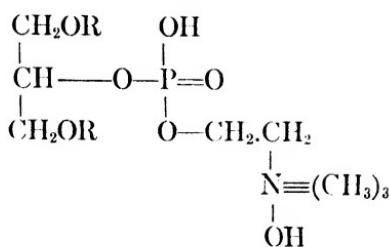
4. With lead acetate T.S., a saturated aqueous solution of Calcium Glycerophosphate yields a white, curdy precipitate, which is soluble in nitric acid.

**Commercial Manufacture.**—(See Sodium Glycerophosphate, p. 186.)

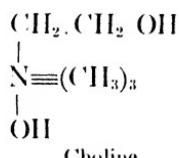
**Pharmaceutical Preparations and Uses.**—1. *Calcium Glycerophosphate* (*Calcii Glycerophosphatas*), N. F. VIII.—This salt "is the normal calcium salt of glycerophosphoric acid and, when dried to constant weight at 130°, contains not less than 98 per cent of  $\text{CaC}_3\text{H}_5(\text{OH})_2\text{PO}_4$ ." This salt is useful chiefly as a source of the calcium ion although the presence of combined phosphorus lends itself to the simultaneous administration of both elements. The use of glycerophosphoric acid salts was originally based on their similarity to lecithins. The lecithins are the esters of fatty acids and glycerophosphoric acid combined with a nitrogenous base (chiefly choline). They occur in animal cells generally combined with proteins. When administered orally they are broken up into glycerophosphates in the intestines. In 1894 Berlow, Pasqualis and Robin suggested that the direct administration of glycerophosphates (calcium and sodium) might produce the same results as obtained by using lecithin. Despite the facts that glycerophosphoric acid is so similar to a part of the lecithin structure (see below), and that the phosphorus of the lecithin of foods is changed into glycerophosphoric acid before being assimilated, Willstaetler claims that synthetic glycerophosphoric acid is not the same as that formed by the decomposition of lecithin. It is generally conceded that the real usefulness and value of glycerophosphates is still very much in doubt.



### Glycerophosphoric acid



### Lecithin



## Choline

Average dose—0.3 Gm. (approximately 5 grains).

2. *Calcium and Sodium Glycerophosphates Elixir* (Elixir Calcii et Sodii Glycerophosphatum, Glycerophosphates Elixir), N. F. VIII.—In addition to other ingredients, this elixir contains 0.9 per cent of calcium glycerophosphate together with 1.8 per cent of sodium glycerophosphate. (See also p. 186.) Average dose—4 cc. (approximately 1 fluidrachm).

3. *Compound Glycerophosphates Elixir* (Elixir Glycerophosphatum Compositum, Compound Glycerophosphates Solution), N. F. VIII.—This elixir contains 1.6 per cent of calcium glycerophosphate together with other glycerophosphates, etc. (See also p. 188.) Average dose—8 cc. (approximately 2 fluidrachms).

## CALCIUM HYDROXIDE

### *Calcium Hydroxide, U. S. P. XIII*

Formula,  $\text{Ca}(\text{OH})_2$ . Molecular Weight, 74.10

**Physical Properties.**—Calcium Hydroxide occurs as a soft, white, crystalline powder, possessing an alkaline, slightly bitter taste. One Gm. of it dissolves in 630 cc. of water at 25° C., and in 1300 cc. of boiling water. It is soluble in glycerin and in syrup, but is insoluble in alcohol.

**Chemical Properties.**—When mixed with three or four times its own weight of water, it forms a smooth magma called "Milk of Lime." This is different from "Lime Water" which is a clear, saturated aqueous solution of calcium hydroxide.

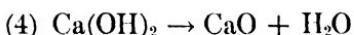
Calcium hydroxide solutions are fairly basic in reaction and are capable of neutralizing acids, *e. g.*, hydrochloric acid, with the formation of the corresponding calcium salt (1). As a special type of neutralizing action one may consider the ability of calcium

hydroxide to absorb carbon dioxide with the formation of calcium carbonate (2, 3).

- (1)  $\text{Ca}(\text{OH})_2 + 2\text{HCl} \rightarrow \text{CaCl}_2 + 2\text{H}_2\text{O}$
- (2)  $\text{H}_2\text{O} + \text{CO}_2 \rightleftharpoons \text{H}_2\text{CO}_3$
- (3)  $\text{Ca}(\text{OH})_2 + \text{H}_2\text{CO}_3 \rightarrow \text{CaCO}_3 \downarrow + 2\text{H}_2\text{O}$

This property of calcium hydroxide is exerted either in the solid form (requiring a little moisture) (see Soda Lime) or in the form of a solution.

When strongly heated, calcium hydroxide loses water and is converted into calcium oxide (4).



**Official Tests for Identity.**—1. When mixed with water to form "Milk of Lime" and allowed to stand, it settles to give a clear supernatant liquid. This liquid is distinctly alkaline to litmus.

2. When calcium hydroxide is dissolved with acetic acid the resulting solution gives all the tests for *Calcium* (*q. v.*).

**Commercial Manufacture.**—Calcium hydroxide, commonly known as "hydrated lime," is made by the careful addition of a limited amount of water to lime (CaO). This process is known as "slaking" and is characterized by the avid absorption of water by the oxide to form calcium hydroxide (5) accompanied by the evolution of much heat, swelling of the CaO lumps and a final disintegration into a fine, white powder. Of course, the quality of the finished product depends upon the purity of the original limestone used to make the CaO. Several grades of calcium hydroxide are produced commercially.



**Pharmaceutical Preparations and Uses.**—1. *Calcium Hydroxide* (Calcii Hydroxidum, Slaked Lime), U. S. P. XIII.—"Calcium Hydroxide contains not less than 95 per cent of  $\text{Ca}(\text{OH})_2$ ." The medicinal and pharmaceutical applications of calcium hydroxide depend upon both the alkalinity (and consequent saponifying power) and the calcium-ion content of the compound. Internally, a solution of it is used as an antacid. The solution is often added to babies' formulæ for the purpose of preventing curdling of the milk in the presence of acid gastric contents, thus promoting the digestibility of the milk. Occasionally, the solution is used as a source of calcium during pregnancy, etc., but there are more efficient and more pleasant ways of ingesting the required amount of calcium.

Inasmuch as calcium hydroxide has potentially a fairly high concentration of hydroxyl ions, it is used in many pharmaceutical preparations as a saponifying agent for oils; in many cases to permit of better mixing of other ingredients in the oily preparations. In addition, calcium hydroxide is mildly astringent.

2. *Calamine Lotion* (*Lotio Calaminae*), U. S. P. XIII.—This preparation contains 80 Gm. each of calamine and zinc oxide, 20 cc. of glycerin, 400 cc. of bentonite magma and sufficient calcium hydroxide solution to make 1000 cc. of finished lotion. The use of calcium hydroxide solution as the diluent instead of distilled water undoubtedly adds mild astringent properties to the lotion. The lotion is used as a protective and mild astringent in various skin eruptions.

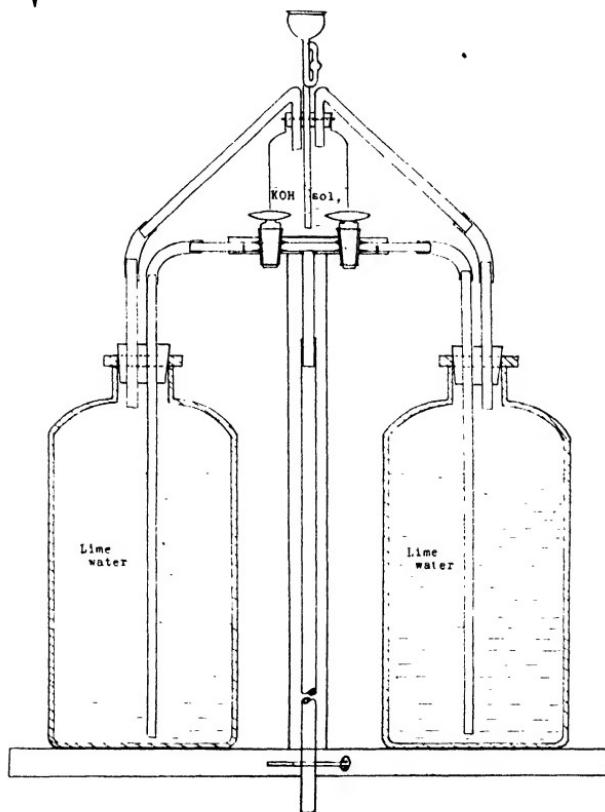


FIG. 15.—Lime water apparatus.

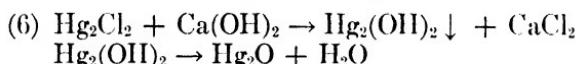
3. *Calcium Hydroxide Solution* (*Liquor Calcii Hydroxidi*, *Liquor Calcis*, Lime Water), U. S. P. XIII.—This "is a solution containing, in each 100 cc., at 25° not less than 0.14 Gm. of  $\text{Ca}(\text{OH})_2$ . The content of calcium hydroxide varies with the temperature at which the solution is stored, being about 0.17 Gm. per 100 cc. at 15°, and less at a higher temperature." It may be prepared by adding 3 Gm. of calcium hydroxide to 1000 cc. of cool distilled water. The mixture is agitated vigorously and repeatedly for one hour, and then the excess calcium hydroxide is allowed to settle. When the solution is dispensed, it is decanted from the settled residue and filtered if necessary.

A convenient apparatus for dispensing and at the same time protecting lime water from atmospheric carbon dioxide is shown in Figure 15. The solution of calcium hydroxide may be syphoned out of either of the two large bottles. All air entering these bottles is freed of carbon dioxide by passing it through a strong solution of KOH contained in the small bottle. When one of the large bottles is emptied, it may be disconnected from the system and used for making additional lime water. During this time the supply is drawn from the other bottle.

Because of the tendency for lime water to react with carbon dioxide in the air to form insoluble calcium carbonate it is desirable to protect it in storage. The undissolved residue in the bottle is not suitable for preparing additional quantities of Calcium Hydroxide Solution. The uses of this preparation have been discussed previously. Average dose—15 cc. (approximately 4 fluidrachms).

4. *Soda Lime* (Calx Soda), U. S. P. XIII.—(See Sodium Hydroxide, p. 191.)

5. *Black Lotion* (Lotio Nigra, Black Wash, Aqua Phagedænica Nigra), N. F. VIII.—This preparation is made by suspending mercurous chloride (9 Gm.) in water (100 cc.) with acacia (1 Gm.). This suspension is then added with stirring to Calcium Hydroxide Solution to give a black precipitate of mercurous oxide (6). The lotion should be prepared at the time of dispensing otherwise the precipitate tends to coagulate into larger particles. ¶ The preparation is used as an antiseptic wash. ¶



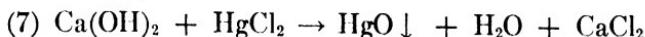
6. *Calamine Liniment* (Linimentum Calaminae), N. F. VIII.—This liniment contains 80 Gm. each of calamine and zinc oxide, 500 cc. of olive oil and sufficient lime water to make 1000 cc. In this preparation calcium hydroxide exercises a saponifying action and also contributes a mild astringency to the liniment.

7. *Lime Liniment* (Linimentum Calcis, Carron Oil), N. F. VIII.—This liniment contains 500 cc. each of calcium hydroxide solution and linseed oil. The two components are simply mixed by agitation to form a creamy, yellow colored liniment. ¶ This preparation is a burn treatment of long standing. ¶

8. *Neocalamine Liniment* (Linimentum Neocalaminae), N. F. VIII.—This liniment contains 150 Gm. of Prepared Neocalamine, 500 cc. of olive oil and enough calcium hydroxide solution to make 1000 cc. of liniment. The function of the calcium hydroxide solution is as a saponifying agent upon the olive oil to provide better suspending properties for the Prepared Neocalamine. (See p. 378.)

9. *Yellow Lotion* (Lotio Flava, Yellow Wash), N. F. VIII.—This lotion is prepared by dissolving 3 Gm. of mercury bichloride in water and adding this solution gradually, with stirring, to enough calcium hydroxide solution to make 1000 cc. of finished preparation. The reaction that takes place (7) results in the formation of yellow

mercuric oxide. ¶The preparation is used for the antiseptic action of the mercury.¶



**10. Zinc Oxide Soft Paste** (*Pasta Zinc Oxidi Mollis, Unna's Soft Zinc Paste*), N. F. VIII.—This preparation contains 25 per cent each of  $\text{ZnO}$ ,  $\text{CaCO}_3$  and linseed oil, 2.5 per cent of oleic acid and sufficient calcium hydroxide solution to make 1000 Gm. of finished product. The calcium hydroxide is used for its saponifying action in this preparation.

### CALCIUM HYPOPHOSPHITE

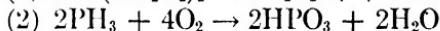
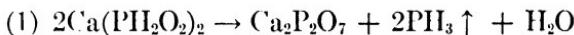
*Calcium Hypophosphite*, N. F. VIII

Formula,  $\text{Ca}(\text{H}_2\text{PO}_2)_2$ . Molecular Weight, 170.07

**Physical Properties.**—Calcium hypophosphite occurs as a white, crystalline powder, and as colorless, transparent, monoclinic prisms, and as thin flexible scales having a pearly luster. It is odorless and has a bitter, nauseous taste. It is stable in air.

Calcium hypophosphite is slowly soluble in about 6.5 parts of water at  $25^\circ \text{ C}$ . It is slightly more soluble in boiling water. The salt is insoluble in alcohol.

**Chemical Properties.**—When calcium hypophosphite is heated above  $300^\circ \text{ C}$ ., it decrepitates and gives off water, phosphine, and spontaneously inflammable dihydrogen phosphide (2). Upon complete ignition, calcium pyrophosphate remains as a residue (1).



Because of the readiness with which hypophosphites are oxidized, this salt, in common with other hypophosphites, should not be heated or triturated with chlorates, nitrates, permanganates, or other oxidizing agents for fear of causing an explosion.

The chemical reactivity of this compound is embodied in the properties of the hypophosphite ion (*q. v.*) and the calcium ion (*q. v.*).

**Official Tests for Identity.**—1. A 1 in 20 aqueous solution of Calcium Hypophosphite responds to the tests for *Calcium* (*q. v.*) and *Hypophosphite* (*q. v.*).

**Commercial Manufacture.**—Calcium hypophosphite is prepared by the action of phosphorus upon milk of lime (3). In order to minimize the loss of phosphorus as hydrogen phosphide and calcium phosphate, partially oxidized phosphorus, made by treating phosphorus under water with atmospheric oxygen, is mixed with milk of lime and heated to about  $55^\circ \text{ C}$ . When all of the spongy appearing phosphorus has disappeared, the mixture is filtered, the residue washed thoroughly with water and the filtrate and washings either evaporated carefully under reduced pressure and with constant

stirring to dryness on a water-bath, or concentrated to the crystallizing point.



**Pharmaceutical Preparations and Uses.**—1. *Calcium Hypophosphate* (*Calcii Hypophosphis*), N. F. VIII.—“Calcium Hypophosphate, when dried for 24 hours over sulfuric acid, contains not less than 98 per cent of  $\text{Ca}(\text{H}_2\text{PO}_2)_2$ .” The only therapeutic value possessed by this salt lies in the calcium ion. It may be used as a source of calcium. The hypophosphate portion of the molecule, as previously shown, is of little value in treating “nerve disorders and wasting diseases” for which it has been proposed. Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains).

2. *Hypophosphites Syrup* (*Syrupus Hypophosphitum*), N. F. VIII.—This syrup contains 3.5 per cent of calcium hypophosphate in addition to varying quantities of other hypophosphites. (See p. 197.) Average dose—8 cc. (approximately 2 fluidrachms).

3. *Compound Hypophosphites Syrup* (*Syrupus Hypophosphitum Compositus*), N. F. VIII.—This preparation contains 3.5 per cent of calcium hypophosphate in addition to other hypophosphites and various other ingredients. Average dose—8 cc. (approximately 2 fluidrachms).

### CALCIUM LACTATE

#### *Calcium Lactate*, U. S. P. XIII

Formula,  $\text{Ca}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 5\text{H}_2\text{O}$ ;  $(\text{CH}_3\text{CH}(\text{OH})\text{COO})_2\text{Ca} \cdot 5\text{H}_2\text{O}$

Molecular Weight, 308.30

**Physical Properties.**—Calcium Lactate occurs as a nearly odorless and tasteless white powder. It effloresces slightly and when heated at  $120^\circ \text{ C}.$ , it loses its 5 molecules of water and becomes anhydrous.

One Gm. of calcium lactate dissolves in 20 cc. of water at  $25^\circ \text{ C}.$ . It is very soluble in hot water. It is nearly insoluble in alcohol.

**Chemical Properties.**—The chemical properties of calcium lactate are those of the calcium ion (*q. v.*) and the lactate ion. (See Sodium Lactate, p. 200.)

**Official Tests for Identity.**—1. A solution of Calcium Lactate (1 in 20) responds to the tests for *Calcium* (*q. v.*) and *Lactate* (*q. v.*).

**Commercial Manufacture.**—Calcium lactate may be made by neutralizing a hot solution of lactic acid with calcium carbonate, filtering, and allowing the salt to crystallize from the filtrate.

Large quantities of the salt are obtained by mixing a solution of a monosaccharide ( $\text{C}_6\text{H}_{12}\text{O}_6$ ) with milk and chalk and inducing lactic acid fermentation by the addition of putrid cheese, which is rich in lactic acid bacilli (1) (2). The mixture is digested for several weeks at a temperature of about  $30^\circ \text{ C}.$  The calcium lactate thus obtained is purified by recrystallization. It is worthy of note that the lactic acid bacillus is very sensitive to free acid, hence the necessity of immediately neutralizing any lactic acid produced. The fer-

mentation period should be comparatively short (two weeks or so), and thus eliminate the danger of the calcium lactate being converted into calcium butyrate through the agency of butyric acid ferment.



**Pharmaceutical Preparations and Uses.**—1. *Calcium Lactate* (*Calcii Lactas*), U. S. P. XIII.—“Calcium Lactate, when dried to constant weight at 120°, contains not less than 98 per cent of  $\text{Ca}(\text{C}_3\text{H}_5\text{O}_3)_2$ .” It is used orally and parenterally for the action of the calcium ion. It is much less irritating than calcium chloride, although it is said to be more irritating than calcium gluconate. Average dose—1 Gm. (approximately 15 grains).

2. *Calcium Lactate Tablets* (*Tabellæ Calcii Lactatis*), N. F. VIII.—These tablets “contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of  $\text{Ca}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 5\text{H}_2\text{O}$ .” The tablets are a convenient form of calcium lactate for oral administration. Average dose—0.3 Gm. (approximately 5 grains) of Calcium Lactate.

## CALCIUM LEVULINATE

### *Calcium Levulinate*, N. F. VIII

Formula,  $(\text{CH}_3\text{CO})(\text{CH}_2)_2\text{COO}_2\text{Ca} \cdot 2\text{H}_2\text{O}$   
Molecular Weight, 306.32

**Physical Properties.**—This salt occurs as a white, crystalline or amorphous powder, having a faint odor suggesting burnt sugar and a bitter, salty taste.

It is freely soluble in water, and slightly soluble in alcohol. It is insoluble in ether and chloroform.

**Chemical Properties.**—Aqueous solutions of this salt are practically neutral. Heating of the salt results in charring of the compound, and further strong heating causes the final formation of calcium oxide as a residue. The important reactions of this salt are those of the calcium ion.

**Official Tests for Identity.**—1. An aqueous solution (1 in 10) of the salt responds to the tests for *Calcium* (*q. v.*).

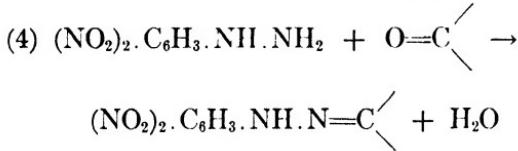
2. Five cc. of a 1 in 10 aqueous solution of the salt is made alkaline with 5 cc. of sodium hydroxide T.S. (1) and the mixture filtered. To the filtrate is added 5 cc. of iodine T.S. which causes the formation of a yellow precipitate of iodoform having a characteristic odor. This reaction is a characteristic one for the detection of any compound possessing, or capable of forming in the reaction,

|  
the  $\text{CH}_3\text{C}=\text{O}$  group. Upon addition of iodine in alkaline solution to compounds of this type the three hydrogens on the methyl group

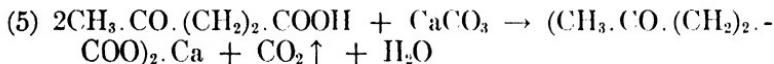
are replaced with iodine (2) and the iodinated carbon then splits off to form iodoform (3).

- (1)  $(\text{CH}_3\text{CO} \cdot (\text{CH}_2)_2 \cdot \text{COO})_2 \cdot \text{Ca} + 2\text{NaOH} \rightarrow 2\text{CH}_3 \cdot \text{CO} \cdot (\text{CH}_2)_2 \cdot \text{COONa} + \text{Ca}(\text{OH})_2$
- (2)  $\text{CH}_3 \cdot \text{CO} \cdot (\text{CH}_2)_2 \text{COONa} + 3\text{NaOI} \rightarrow \text{Cl}_3 \cdot \text{CO} \cdot (\text{CH}_2)_2 \cdot \text{COONa} + 3\text{NaOH}$
- (3)  $\text{Cl}_3 \cdot \text{CO} \cdot (\text{CH}_2)_2 \text{COONa} + \text{NaOH} \rightarrow \text{CHI}_3 \downarrow + (\text{CH}_2)_2 \cdot (\text{COONa})_2$

3. One-tenth Gm. of the salt when dissolved in 2 cc. of distilled water and treated with 5 cc. of dinitrophenylhydrazine T.S. forms a dinitrophenylhydrazone on standing in an ice-bath for one hour. The hydrazone melts between 198° and 206° C. This reaction is one which is characteristic of the carbonyl group () one of which occurs in calcium levulinate (4).



**Commercial Manufacture.**—This compound is prepared by the interaction of levulinic acid with calcium carbonate (5) or milk of lime. Levulinic acid is obtainable commercially although it can also be made by heating various sugars with acid.



**Pharmaceutical Preparations and Uses.**—1. *Calcium Levulinate* (Calcii Levulinatas), N. F. VIII.—This salt “is a hydrated calcium salt of levulinic acid and contains not less than 97.5 per cent and not more than 100.5 per cent of  $(\text{CH}_3 \cdot \text{CO} \cdot (\text{CH}_2)_2 \text{COO})_2 \cdot \text{Ca}$  calculated on a dry basis, the loss on drying being determined on a separate portion by drying at 105° for 24 hours.” Calcium levulinate is another of the organic acid salts of calcium having a less irritating action than calcium chloride. In addition, calcium levulinate has the advantage of being more water-soluble than many of the others, thus enabling it to be used in more highly concentrated solutions. This salt is useful for intravenous and also subcutaneous use.

2. *Calcium Levulinate Ampuls* (Ampullæ Calcii Levulinatis, Calcium Levulinate Injection), N. F. VIII.—These ampuls “contain a sterile solution of calcium levulinate in water for injection, and yield not less than 95 per cent and not more than 105 per cent of the labeled amount of  $(\text{C}_5\text{H}_7\text{O}_3)_2 \cdot \text{Ca} \cdot 2\text{H}_2\text{O}$ .” It is used for the purposes stated above. Average dose—1 Gm. of Calcium Levulinate.

**CALCIUM OXIDE***Lime, N. F. VIII*

Formula, CaO. Molecular Weight, 56.08

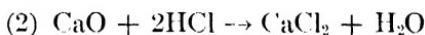
**Physical Properties.**—This compound occurs as hard, white or grayish-white masses or granules, or a white powder. It is odorless but has a burning caustic taste.

One Gm. of Lime is soluble in about 840 cc. of water at 25° C., and in about 1740 cc. of boiling water. It is soluble in syrup and glycerin, but is insoluble in alcohol.

**Chemical Properties.**—Calcium oxide slowly absorbs moisture and carbon dioxide from the air, to form "air-slaked" lime. It unites vigorously with water (1) as previously described (see Calcium Hydroxide, p. 327) to form calcium hydroxide (slaked lime).



When dissolved in water, its actions are those of calcium hydroxide and when dissolved in acids (2) it responds to the reactions for calcium ion.



**Official Tests for Identity.**—1. When lime is moistened with water heat is generated and a white powder is obtained. If this powder is mixed with 3 or 4 times its own weight of water it forms a smooth magma known as "Milk of Lime" which is alkaline to litmus.

2. When 1 Gm. is slaked with water, and the slaked material dissolved in acetic acid, the solution responds to the tests for Calcium (*q. v.*).

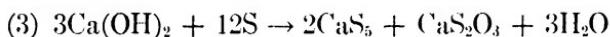
**Commercial Manufacture.**—Calcium oxide is made by calcining a comparatively pure native calcium carbonate, *e. g.*, marble, chalk, or limestone, in a suitable kiln. One of the newer forms of lime kilns consists of a vertical cylinder of steel or masonry lined with fire brick, and heated by fire boxes located near the base of the kiln. The kiln is arranged so that the entire charge of limestone is exposed to the heated products of combustion of a fuel, without actually coming in contact with them. The carbon dioxide (see V. D. of CO<sub>2</sub>, 1.5; air = 1) is removed from the kiln by a current of air entering at the bottom. Large quantities of lime are being made in rotary furnaces or kilns.

Native calcium carbonates contain natural occurring impurities, *e. g.*, magnesia, oxides of iron, silica, and clay. When clay is present in excessive amounts, a quicklime is obtained that slakes only feebly or not at all. Such a product is called "over-burnt lime" and is not fit for use.

**Pharmaceutical Preparations and Uses.**—1. *Lime* (Calx, Calcium Oxide, Quicklime), N. F. VIII.—"Lime, when freshly ignited to constant weight with a blast lamp, contains not less than 95 per cent of CaO." Lime, as such, is not used internally. Calcium

oxide is used in making various insecticides (see Bordeaux Mixture) and is a constituent of many fertilizers. Most specifications for the above preparations, however, call for hydrated lime (calcium hydroxide). Because of its cheapness, lime is of great commercial importance, being used in making mortar, which consists of lime and sand, to which is added, with stirring, enough water to make a paste. When mortar is exposed to air it loses water and absorbs carbon dioxide and is slowly converted to a porous mass. This hardening process is known as "setting."

2. *Sulfurated Lime Solution* (*Liquor Calcis Sulfuratae*, Vleminckx' Solution, Vleminckx' Lotion), N. F. VIII.—This preparation requires 165 Gm. of Lime and 250 Gm. of Sublimed Sulfur together with enough water to give 1000 cc. of preparation. The lime is slaked and then boiled with the sulfur in 1750 cc. of water. The volume is reduced to 1000 cc. and maintained there, while boiling, for one hour by the addition of water from time to time. Finally, the mixture is cooled and filtered. The reaction probably is represented by this equation (3):



This clear, brownish-red liquid is useful in treating acne and many other skin diseases, its action being that of sulfides in general.

### DIBASIC CALCIUM PHOSPHATE

#### *Dibasic Calcium Phosphate*, U. S. P. XIII

Formula,  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ . Molecular Weight, 172.20

**Physical Properties.**—This salt occurs as a white, odorless, and tasteless powder which is stable in air.

It is almost insoluble in water but is soluble in diluted hydrochloric and nitric acids. It is insoluble in alcohol.

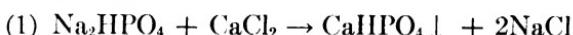
**Chemical Properties.**—This salt is rather insoluble in water and, therefore, its chemical reactions are few and relatively unimportant. Solutions of the salt in acids respond to the reactions of calcium and phosphate.

It is interesting to note that the nomenclature of this compound, *i. e.*, *dicalcium* phosphate as it is commonly known, is somewhat confusing in that one would normally look for two calciums instead of the one which actually is present. In this case, the prefix *di* refers to the number of hydrogens which have been replaced rather than to the number of calcium atoms present.

**Official Tests for Identity.**—1. Dibasic calcium phosphate, when dissolved in diluted hydrochloric acid, gives a solution which will react with ammonium oxalate T.S. to give a white precipitate of calcium oxalate (see p. 313).

2. The salt, when dissolved with the aid of a slight excess of nitric acid, gives the usual test for phosphate with an excess of ammonium molybdate T.S. (see p. 314).

**Commercial Manufacture.**—Dibasic calcium phosphate is usually prepared as a white, flocculent precipitate by the interaction of secondary sodium phosphate and calcium chloride in a neutral solution (1). It is necessary that the solution be neutral since an ammoniacal solution of the same reactants will precipitate tribasic calcium phosphate (see p. 314).



**Pharmaceutical Preparations and Uses.**—1. *Dibasic Calcium Phosphate* (*Calcii Phosphas Dibasicus, Dicalcium Orthophosphate*). U. S. P. XIII.—This salt “contains an amount of calcium equivalent to not less than 98 per cent of  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ .” It is also known commonly as “dibasic calcium phosphate.” Because it provides an optimum ratio of calcium to phosphorus, namely 1 to 1, this is the calcium salt most frequently recommended for oral consumption. It is stated by some workers that the greater the difference between the intake levels of the two minerals (calcium and phosphorus) the less satisfactory is the absorption. Because of the fact that this salt supplies both calcium and phosphorus, it is said to be especially valuable for bone growth in children, pregnant women and lactating mothers. It is supplied either with or without vitamin D, which favors better utilization of the salt. Average dose—1 Gm. (approximately 15 grains).

### TRIBASIC CALCIUM PHOSPHATE

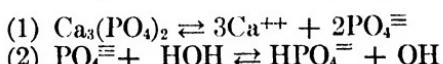
*Tribasic Calcium Phosphate*, N. F. VIII

Formula,  $\text{Ca}_3(\text{PO}_4)_2$ . Molecular Weight, 310.20

**Physical Properties.**—Precipitated calcium phosphate is a bulky white, amorphous or microcrystalline powder. It is odorless and tasteless. Its specific gravity is 3.14 at  $\frac{2}{4}^{\circ}\text{C}$ . The salt is stable in air. At  $1670^{\circ}\text{C}$ . the salt fuses without decomposition.

Precipitated calcium phosphate is almost insoluble in water and is decomposed slightly by boiling water. It is insoluble in alcohol. The salt readily dissolves in diluted nitric or hydrochloric acids. Except when freshly precipitated, it is almost insoluble in acetic acid.

**Chemical Properties.**—This compound is even more insoluble than dibasic calcium phosphate, and consequently has few chemical reactions. It is interesting to note, however, that the salt is an antacid and is used as such in therapy. The antacid action is dependent upon the phenomenon of hydrolysis of the phosphate ion. Calcium phosphate is classed as an insoluble salt but all salts in contact with a solvent ionize to a slight extent (1). The phosphate ion is a fairly strong base and is extensively hydrolyzed in aqueous solutions to give the secondary phosphate ion and hydroxyl ion (2).

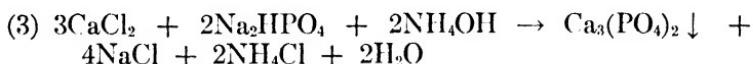


The hydroxyl ion, of course, will react with acidic hydrogens which are introduced (from hydrochloric acid, for example) to form undissociated water. This disturbs the equilibrium and causes more of the calcium phosphate to ionize to furnish more phosphate, etc.

**Official Tests for Identity.**—1. When the salt is dissolved in nitric acid, the solution will give a precipitate of ammonium phosphomolybdate (yellow) when treated with ammonium molybdate T.S.

2. The salt gives a characteristic flame test for calcium.

**Commercial Manufacture.**—Tribasic Calcium Phosphate is usually prepared by the mutual decomposition of calcium chloride and secondary sodium phosphate in the presence of ammonia water, which decreases hydrolysis and thereby minimizes the formation of secondary calcium phosphate ( $\text{CaHPO}_4$ ) (3).

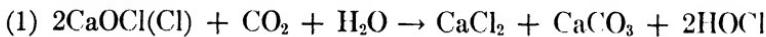


The white precipitate is washed with hot water until free from chlorides and dried at 100° C.

**Pharmaceutical Preparations and Uses.**—1. *Tribasic Calcium Phosphate* (*Calcii Phosphas Tribasicus*, Precipitated Calcium Phosphate), N. F. VIII.—“Tribasic Calcium Phosphate, after ignition to constant weight, contains an amount of phosphate ( $\text{PO}_4$ ) corresponding to not less than 90 per cent of  $\text{Ca}_3(\text{PO}_4)_2$ .” Although this salt may be used as a source of calcium (especially when both calcium and phosphorus are desired) it is less effective than the dibasic form. However, it is a valuable gastric antacid. Average dose—1 Gm. (approximately 15 grains).

#### NON-OFFICIAL CALCIUM COMPOUNDS

**Bleaching Powder** (Chlorinated Lime, Chloride of Lime),  $\text{CaOCl(Cl).H}_2\text{O}$ .—Bleaching powder is a white or grayish-white, granular powder, having a distinct odor of chlorine and hypochlorous acid. It is partially soluble in water and in alcohol. *It is not deliquescent.* When it is exposed to the air it slowly decomposes (1).



Bleaching powder is a product resulting from the action of chlorine upon calcium hydroxide and is best represented by the formula,  $\text{CaOCl(Cl).H}_2\text{O}$ . The idea that this substance is an equimolecular mixture of calcium chloride and calcium hypochlorite is erroneous because bleaching powder does not possess the properties of the admixed salts and, furthermore, although it does become moist upon exposure to air, it does not deliquesce.

The method used today for manufacturing bleaching powder is the same as that employed by Tennant and Knox at Glasgow in 1799. Thoroughly slaked lime is spread upon shelves in a box-like container and subjected to the action of chlorine (gas), which is introduced at the top of the chamber and “flows” down over and

through the contents of the shelves. The temperature of the absorption vessel is maintained below 25° C., thus minimizing the formation of calcium chlorate. When the absorption of chlorine is complete, powdered lime is blown into the chamber to take up any excess chlorine.

This preparation was recognized in the U. S. P. X as Calx Chlorinata (Chlorinated Lime). Its last official recognition was as a reagent under the Reagent Standards in the U. S. P. XII, p. 666. It is used today principally for its disinfecting properties and as a bleaching agent.

**Calcium Sulfate** (Gypsum),  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ , Molecular Weight, 172.17.—Calcium sulfate with 2 molecules of water of hydration ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ) occurs abundantly and widely distributed in Nature. It is found as well-defined monoclinic prisms as *gypsum* and *selenite* and in granular, semi-opaque masses called *alabaster*. Rhombic prisms of anhydrous calcium sulfate are found as the mineral *anhydrite*. Calcium sulfate ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ) is a constituent of most permanently hard water (*q. v.*).

The dihydrate ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ) is only sparingly soluble in water, its solubility increasing with rising temperatures to a maximum at 40° C. and then decreasing. One Gm. is soluble in about 500 cc. of water at 18° C., but it requires about 650 cc. of boiling water to effect solution. It is insoluble in alcohol, in ether and in chloroform.

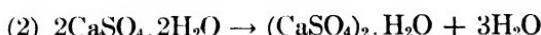
$\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$  may be prepared artificially by adding a soluble sulfate to a solution of a calcium salt (1). The white, crystalline precipitate is washed thoroughly with hot water and dried.



Calcium sulfate ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ) is never used in internal medicine. A mixture of gypsum, clay, and sand is known as *gypsite* and is used for making wall plaster. *Alabaster* is used for ornamental work. *Gypsum* is employed as a filler for wall paper. Possibly its most important use is in the manufacture of *Plaster of Paris*.

*Plaster of Paris* is a white or grayish-white powder, odorless and tasteless, which, when mixed with water, forms a plastic mass that quickly "sets" or hardens. The "setting" is always accompanied by a very slight expansion, and, therefore, it is especially adapted for taking impressions of moulds, etc. The final product is a white solid consisting of myriad crystals of more highly hydrated calcium sulfate. Plaster of Paris slowly attracts water from moist air, becomes granular and loses its property of setting when mixed with water.

When gypsum is heated to about 125° C. it loses three-fourths of its water of hydration and forms the hemihydrate (2).



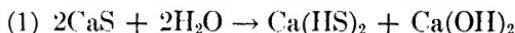
Great care is exercised so as not to "over-heat" the gypsum, as this results in a product that sets so slowly and imperfectly as to make it unfit for use as Plaster of Paris.

It may be prepared in the laboratory as follows: In a tared, small porcelain evaporating dish, heat 20 Gm. of gypsum on a sand-bath at a temperature not exceeding 125° C. until it weighs 16.86 Gm., stirring occasionally during the heating. Take a portion (5 Gm.) of the product, mix to a thick paste with water, and mould it into a cube or ball.

Plaster of Paris is used in surgery for making casts. In dentistry, it is employed for taking impressions. It is used in the industries as a cement, for stucco work, for making building blocks, for "plastering" wines, etc.

**Calcium Sulfide** (Calcium Monosulfide), CaS, Molecular Weight, 72.14.—Calcium sulfide is a pale yellow or grayish-white solid. It has an odor of hydrogen sulfide and possesses a strong, offensive, alkaline taste.

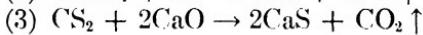
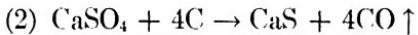
The salt is almost insoluble in water, but is gradually hydrolyzed into calcium hydrogen sulfide and calcium hydroxide (1), both of which are more soluble than the normal salt.



It is insoluble in alcohol, but soluble in aqueous solutions of ammonium salts.

In 1750, Marggraf observed that calcium sulfide that had been exposed to sunlight usually phosphoresced in the dark. Since absolutely pure calcium sulfide does not possess this property, it is thought that the phosphorescence may be due to minute traces of bismuth and vanadium salts.

Calcium monosulfide may be made by reducing calcium sulfate with charcoal (2), or by passing the vapor of carbon disulfide and carbon dioxide over incandescent lime (3).



This salt is used to make luminous paints. A solution, containing the products resulting from the hydrolysis of CaS (*q. v.*), is an excellent solvent for hair and wool.

A crude form of calcium sulfide was formerly official (U. S. P. IX) under the title *Calcii Sulphidum Crudum*. It is known also as *Sulfurated Lime*, *Calcic Liver of Sulfur*, and *Hepar Calcis*. It was a grayish-white, sometimes yellowish powder, having an odor of hydrogen sulfide and a nauseous, alkaline taste. It contained not less than 55 per cent of calcium monosulfide.

Usually it was made by heating a mixture of exsiccated calcium sulfate, charcoal, and starch to bright redness in a crucible until the black color had disappeared (4). The mixture was allowed to cool, powdered, and preserved in well-stoppered bottles. The starch facilitated the reduction of the calcium sulfate which, however, was never complete, the final product always containing some unchanged calcium sulfate and carbon in variable amounts.



It may be prepared in the laboratory as follows: Mix thoroughly 35 Gm. of exsiccated calcium sulfate, 5 Gm. of charcoal (in fine powder) and 1 Gm. of starch, and pack the mixture lightly in a porcelain crucible. Cover it loosely and heat to bright redness. Continue the heating until the content has lost its black color. Allow it to cool, powder and bottle immediately.

Crude calcium sulfide is employed internally with doubtful efficacy in the treatment of acne and furunculosis. Average dose— $\frac{1}{4}$  to 1 grain. A paste composed of equal parts of starch and crude calcium sulfide is used as a depilatory. It is often used as a parasiticide in scabies (effecting the solution of the skin and eggs of the mite).

## CHAPTER XIX

### STRONTIUM AND STRONTIUM COMPOUNDS

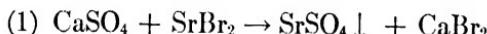
#### STRONTIUM

Symbol, Sr. Valence, II. Atomic Weight, 87.63;  
Atomic Number, 38

**Occurrence.**—Strontium belongs to the alkaline earth family. It is found as the sulfate ( $\text{SrSO}_4$ ) in the mineral, *celestite*, and as carbonate ( $\text{SrCO}_3$ ) in the mineral, *strontianite*. The latter occurs in large quantities in Salzburg, Germany, in Scotland, England, and in Pennsylvania and New York states. In these same countries, *celestite* is found in even greater quantities. In 1807, Davy isolated the element by the electrolysis of the hydroxide and named it *strontium*, from a village (Strontian) in Argyleshire, Scotland, near which the mineral strontianite is found.

**Physical Properties.**—Strontium is a “brass-yellow” metal, having a specific gravity of about 2.6 at  $20^\circ \text{C}$ . It melts at  $800^\circ \text{C}$ . and is not volatilized at higher temperatures. It should be kept under naphtha. The metal is malleable and ductile and burns in air with an intense illumination. Strontium salts impart a red color to a flame. Strontium and its compounds closely resemble calcium in both physical and chemical properties (*q. v.*). The solubilities of strontium salts are between those of barium and calcium.

**Chemical Properties.**—The chemical properties of strontium are almost identical with those of calcium (*q. v.*). However, it is of interest to note that strontium sulfate is much less soluble than is calcium sulfate. This is easily shown by the fact that addition of a solution of soluble strontium salt to a saturated solution of calcium sulfate will produce a precipitate of strontium sulfate (1).



Strontium salts such as the hydroxide, carbonate, nitrate, and the salts of various organic acids yield strontium oxide ( $\text{SrO}$ ) when strongly heated. Calcium salts are more readily converted to the oxide by heating than are the strontium salts.

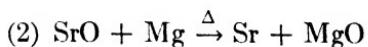
The volatile strontium salts impart a carmine-red color to a non-luminous flame when heated, this being the basis for their use in fireworks, Yule log salts, etc.

**Official Tests for Identity.**—1. Calcium sulfate T.S. will produce a white precipitate of strontium sulfate with solutions of strontium salts (1).

2. When moistened with hydrochloric acid, all strontium salts will impart a crimson color to a non-luminous flame.

**Commercial Manufacture.**—The metal may be made by the electrolysis of the chloride or by heating a saturated solution of strontium

chloride with sodium amalgam and then distilling off the mercury. A mixture of magnesium oxide and metallic strontium is obtained when strontium oxide is heated with magnesium metal (2).



**Pharmacological Action of the Strontium Ion.**—This cation produces effects that closely resemble the characteristic pharmacological actions of calcium ion. However, it is much weaker and also less toxic. It cannot substitute for the calcium ion because withdrawal of calcium and substitution of strontium in its place causes the characteristic symptoms of calcium deficiency.

Some years ago, strontium salts came into prominence because it was thought that by virtue of the combination with the strontium ion, the anions would be more slowly absorbed and therefore, would have a more gradual and a milder action. Krahulik and Pilcher (1918) showed that the rate of absorption of iodide ion from strontium iodide is the same as that from potassium iodide. Blankenhorn (1916) demonstrated also that the "toxic" effects of strontium salicylate were just as great as those produced by sodium salicylate.

For all practical purposes the strontium ion may be considered as a mere carrier for an active anion, *e. g.*, bromide, salicylate, etc.

**Uses.**—Strontium metal is of comparatively little commercial importance.

#### OFFICIAL STRONTIUM COMPOUNDS

##### STRONTIUM BROMIDE

###### *Strontium Bromide, N. F. VIII*

Formula,  $\text{SrBr}_2 \cdot 6\text{H}_2\text{O}$ . Molecular Weight, 355.56

**Physical Properties.**—Strontium Bromide occurs in colorless, transparent, hexagonal crystals. It is odorless, and has a bitter, saline taste. It is deliquescent in moist air, but effloresces in very dry air.

One Gm. of the salt dissolves in about 0.35 cc. of water at 25° C. It is soluble in alcohol but not in ether.

**Chemical Properties.**—The chemical properties of strontium bromide are those of the strontium ion (*q. v.*) and the bromide ion (*q. v.*).

**Official Tests for Identity.**—1. An aqueous solution of the salt (1 in 20) responds to the tests for *Strontium* (*q. v.*).

2. It also responds to the tests for *Bromide* (*q. v.*).

**Commercial Manufacture.**—Strontium Bromide can be prepared by adding strontium carbonate to hydrobromic acid until effervescence has ceased (1). The solution is filtered, concentrated, and allowed to crystallize.



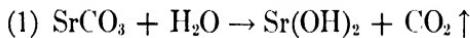
**Pharmaceutical Preparations and Uses.**—1. *Strontium Bromide* (Strontii Bromidum), N. F. VIII.—"Strontium Bromide contains not less than 98 per cent of  $\text{SrBr}_2 \cdot 6\text{H}_2\text{O}$ ." It is used solely for the

sedative effect of the bromide ion, but probably possesses no advantages over any other bromide. Average dose—1 Gm. (approximately 15 grains).

**Strontium Salicylate**, N. F. VIII.—This salt is not discussed because it is an organic compound used almost exclusively for the salicylate ion effect.

#### NON-OFFICIAL STRONTIUM COMPOUNDS

**Strontium Hydroxide** [Sr(OH)<sub>2</sub>].—Strontium hydroxide, like calcium hydroxide, reacts with sucrose to form sparingly soluble compounds (strontium monobasic saccharate [C<sub>12</sub>H<sub>22</sub>O<sub>11</sub>.SrO] and strontium dibasic saccharate [C<sub>12</sub>H<sub>22</sub>O<sub>11</sub>.2SrO], which are readily decomposed by carbon dioxide into sucrose and strontium carbonate). Therefore, it is employed in the sugar industry to precipitate sucrose from beet-sugar molasses. The precipitated strontium carbonate is reconverted into the hydroxide by heating in a current of superheated steam; a process that is used to make the hydroxide from strontianite (1).



Strontium hydroxide is an active base and is soluble in 50 parts of cold water and in 2.1 parts of boiling water. Upon cooling the solution, it crystallizes with 8 molecules of water [Sr(OH)<sub>2</sub>.8H<sub>2</sub>O].

**Strontium Nitrate** [Sr(NO<sub>3</sub>)<sub>2</sub>].—Strontium nitrate is made by dissolving the carbonate in nitric acid. It dissolves in 1.5 parts of water and is slightly soluble in alcohol and in acetone. From hot solutions it separates in the form of anhydrous, regular octahedrons, and from cold solutions monoclinic crystals of the tetrahydrate [Sr(NO<sub>3</sub>)<sub>2</sub>.4H<sub>2</sub>O] are obtained. A mixture of anhydrous strontium nitrate, sulfur, charcoal, and potassium chlorate forms the “red fire” used for pyrotechnic displays.

**The Halides of Strontium.**—The halides of strontium are made by the action of the halogen acids upon strontium carbonate. They are deposited from the solutions as white crystals of the hexahydrates (SrCl<sub>2</sub>.6H<sub>2</sub>O; SrBr<sub>2</sub>.6H<sub>2</sub>O; SrI<sub>2</sub>.6H<sub>2</sub>O) and are very soluble in water. Strontium bromide containing 6 molecules of water of hydration is recognized by the N. F. VIII and has already been discussed.

## CHAPTER XX

### BARIUM AND BARIUM COMPOUNDS

#### **BARIUM**

Symbol, Ba. Valence, II. Atomic Weight, 137.36;  
Atomic Number, 56

**History and Occurrence.**—In 1808 Davy isolated metallic barium by electrolyzing the chloride in the presence of mercury and subsequently decomposing the amalgam.

In combination, barium is widely and abundantly distributed in Nature. As the sulfate ( $\text{BaSO}_4$ ) it occurs in the mineral *barite* or *heavy spar* and as the carbonate ( $\text{BaCO}_3$ ) in the mineral *witherite*. In smaller quantities it also occurs in manganese ores, *e. g.*, *psilomelane*,  $(\text{MnBa})\text{O} \cdot \text{MnO}_2$ , and in combination as the silicate. It is found in sea water, in mineral waters, in marine plants, and in the ashes of some woods, notably those of beech.

**Physical Properties.**—Barium is a silver-white or slightly yellowish-white metal having a specific gravity of 3.5 ( $20^\circ$ ). It melts at  $850^\circ \text{ C.}$ , boils at  $1140^\circ \text{ C.}$ , and is not volatile under ordinary conditions.

**Chemical Properties.**—Upon exposure to air it oxidizes rapidly and hence must be kept under petroleum or other oxygen-free liquids. When placed on water, it acts energetically, liberating hydrogen and forming a solution of the hydroxide which is an active base. The physical and chemical properties of barium compounds closely resemble those of calcium and strontium.

It is interesting to note that just as strontium sulfate is more insoluble than calcium sulfate, barium sulfate is less soluble than either calcium or strontium sulfates. The solubility even in acids is so low that large quantities of barium sulfate can be ingested without untoward reactions; this in spite of the known toxicity of the barium ion.

**Official Tests for Identity.**—1. Solutions of barium salts will yield a precipitate of barium sulfate when treated with diluted sulfuric acid (1).



This precipitate is insoluble in hydrochloric or nitric acids.

2. Barium salts impart a characteristic yellowish-green color to a non-luminous flame. This flame appears blue when viewed through a green glass.

**Commercial Manufacture.**—Metallic barium is made (1) by the electrolysis of the molten chloride or (2) by the electrolysis of an aqueous solution of barium chloride using a mercury cathode. In

the latter method, the barium forms an amalgam with the mercury and the mercury is then removed from the barium by heating in an atmosphere of hydrogen gas.

**Pharmacological Action of Barium Ion.**—Barium ion differs from calcium and strontium ions by being very toxic. Its effects closely resemble those of the digitalis group. Attempts have been made to substitute barium chloride for digitalis, but from a therapeutic standpoint it has been proven decidedly inferior on account of its marked coronary vasoconstriction. However, it has been found very useful in treating special forms of heart disease. Barium ion also produces local irritation. On account of their toxicity, soluble barium compounds or those that may be made soluble by the weak acids of the digestive fluids are not extensively used in therapeutics.

**Uses of Barium.**—Metallic barium is of some use commercially in the manufacture of radio tubes and automobile ignition systems, but is of little pharmaceutical importance.

#### OFFICIAL BARIUM COMPOUNDS

##### BARIUM CHLORIDE

###### *Barium Chloride*, N. F. VIII

Formula,  $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ . Molecular Weight, 244.31

**Physical Properties.**—This compound occurs as white or colorless crystals or as white granules which are odorless.

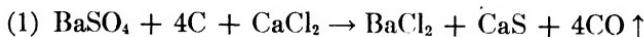
One Gm. of the compound dissolves in about 2.8 cc. of water at 25° C., and in about 1.5 cc. of boiling water. It is insoluble in alcohol, but 1 Gm. dissolves in 8 cc. of glycerin at 25° C.

**Chemical Properties.**—Barium chloride has the reactions of the barium ion (*q. v.*) and of the chloride ion (*q. v.*).

**Official Tests for Identity.**—1. An aqueous solution of the salt responds to all tests for *Barium* (*q. v.*).

2. An aqueous solution also responds to all tests for *Chloride* (*q. v.*).

**Commercial Manufacture.**—Barium Chloride is manufactured by heating heavy spar ( $\text{BaSO}_4$ ) with carbon and calcium chloride (1).



Barium chloride with 2 molecules of water of hydration crystallizes from a concentrated aqueous solution in the form of white, rhombic plates.

**Pharmaceutical Preparations and Uses.**—1. *Barium Chloride* (*Barii Chloridum*), N. F. VIII.—“Barium Chloride contains not less than 99 per cent of  $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ .” The N. F. cautions: *Barium Chloride is extremely poisonous. Internally*, barium chloride has been used in the treatment of Stokes-Adams disease, commonly known as heart-block. To understand the function of barium in the treatment of this disease, one should know that the parts of the heart,

the auricles and ventricles, usually contract and relax harmoniously. However, in the above disease there is a disorganization in the usual harmonious relationship, in that the ventricles contract and relax much more slowly than the auricles. Barium chloride is used to speed up the lagging ventricles, and often produces a dramatic recovery.<sup>1</sup>

Barium chloride has found some use in veterinary medicine as a treatment for constipation in horses, for impaired action of the first stomach of cattle, and as an intestinal peristaltic. One can readily appreciate why a peristaltic action ensues when soluble barium ion contacts smooth muscle if one has ever watched the contractions of a smooth muscle strip in a muscle bath when treated with barium chloride solution. The internal use of barium chloride should be very closely watched because of the toxicity of the compound.

A technical grade of the compound is used as a rat poison, in the leather, textile and ceramic industries, and in the manufacture of some pigments.

2. *Barium Chloride Tablets* (*Tabellæ Barii Chloridi*), N. F. VIII.—These tablets "contain not less than 91 per cent and not more than 109 per cent of the labeled amount of BaCl<sub>2</sub>.2H<sub>2</sub>O." These tablets are intended for veterinary use. Average dose—Horses, 2 Gm. (approximately 30 grains).

## BARIUM SULFATE

### *Barium Sulfate*, U. S. P. XIII

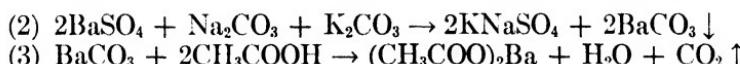
Formula. BaSO<sub>4</sub>. Molecular Weight, 233.42

**Physical Properties.**—Barium Sulfate is a fine, white, odorless, tasteless, bulky powder, free from grittiness.

The salt is insoluble in water, organic solvents, and in dilute acids and alkalies. It is soluble in concentrated sulfuric acid (1).



**Chemical Properties.**—Barium Sulfate is so insoluble that it enters into very few chemical reactions. It can be solubilized by concentrated sulfuric acid (1) or by fusing it with alkali carbonates. An equal mixture of sodium and potassium carbonates is often used to convert the barium sulfate to the carbonate form (2). Once the barium has been converted to the carbonate form it is easily solubilized by the use of acids other than sulfuric, *e. g.*, acetic acid (3).

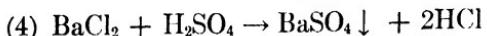


<sup>1</sup> See also, Cohn and Levine: *Arch. Int. Med.*, **36**, 1 (1925). Goodman and Gilman: *Pharmacological Basis of Therapeutics*, New York, Macmillan Pub. Co., p. 608 (1941).

**Official Tests for Identity.**—1. Five-tenths Gm. of barium sulfate is mixed with 2 Gm. each of anhydrous sodium carbonate and potassium carbonate and the mixture fused (2) in a crucible. The fused mixture is then lixiviated with distilled water and filtered. The filtrate gives a test for *Sulfate* (*q. v.*).

2. The residue from the filtration is barium carbonate and when it is dissolved in acetic acid, the solution gives the usual tests for *Barium* (*q. v.*).

**Commercial Manufacture.**—1. Barium sulfate, for Roentgen-ray purposes, is made by precipitating the barium ions from a cold, dilute solution of a soluble barium salt with dilute sulfuric acid (4). The salt is filtered off, thoroughly washed, dried, and screened.



2. Barium sulfate for industrial uses, *e. g.*, making paint, filler for glazed cards, etc., is made by treating a soluble barium salt with sulfuric acid (5). It is also a by-product of several industries, *e. g.*, the manufacture of  $\text{H}_2\text{O}_2$  from  $\text{BaO}_2 \cdot 8\text{H}_2\text{O}$  and  $\text{H}_2\text{SO}_4$ . The industrial grade of barium sulfate should never be administered internally.

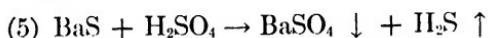


FIG. 16.—Roentgen-ray photograph of stomach before taking barium sulfate.

**Pharmaceutical Preparations and Uses.**—1. *Barium Sulfate* (Barii Sulfas), U. S. P. XIII.—Barium Sulfate should be free from soluble barium compounds. On account of the danger of confusing the poisonous sulfide and sulfite with the sulfate, the U. S. Pharmacopœia cautions physicians who desire to prescribe the latter against abbreviating the word "sulfate." It has been observed that the

absorption coefficients of elements for Roentgen-rays are directly proportional to the number of electrons in the respective atoms. Therefore, it may be correctly assumed that the atomic weight of an element is a criterion of its worth in absorbing Roentgen-rays. Because of the relatively high atomic weight of barium and because of the insolubility of barium sulfate in dilute acids and alkalies (thereby eliminating barium ion action), this compound is of great value in Roentgen-ray diagnosis (Figs. 16 and 17). It has a distinct advantage over bismuth compounds because it does not delay the gastric movements and, furthermore, it is less expensive. One hundred to 150 Gm., when mixed with about 2 and a half times its weight of corn meal mush flavored with cocoa, may be given with impunity. A rather thin magma of barium sulfate may also be injected rectally.

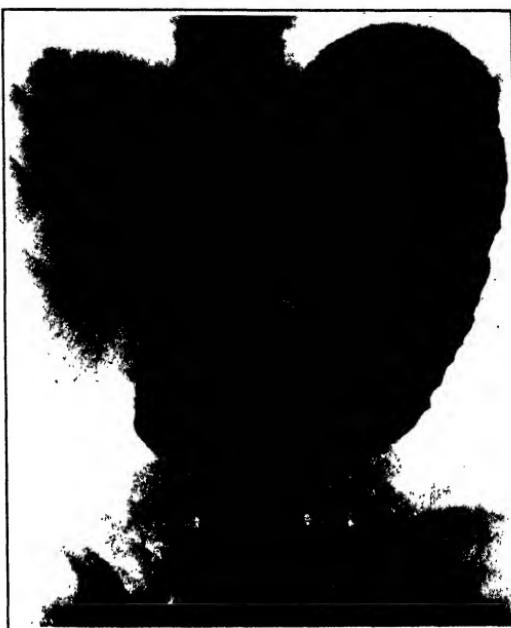


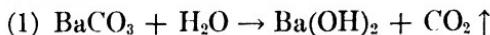
FIG. 17.—Roentgen-ray photograph of stomach after taking barium sulfate.

Commercial barium sulfate ("Blanc Fixe," "permanent white") is used for making lithopone paints, paper fillers, sizes, modifying colors of pigments, etc. The commercial grade should never be used for Roentgen-ray work as it usually contains poisonous soluble barium salts.

#### NON-OFFICIAL BARIUM COMPOUNDS

**Barium Hydroxide** [Ba(OH)<sub>2</sub>.8H<sub>2</sub>O].—Barium hydroxide (Caustic Baryta) occurs as white or colorless crystals which are more soluble in water (1 to 15) than the hydroxides of either calcium or strontium. It is an active base. Its aqueous solution is known as "*baryta water*."

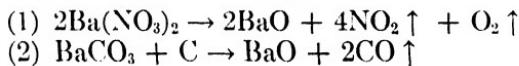
It is made by the action of barium oxide on water or by the action of superheated steam on barium carbonate (1).



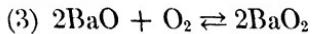
The octahydrate,  $\text{Ba}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$ , crystallizes from an aqueous solution of  $\text{Ba}(\text{OH})_2$ . When carbon dioxide is passed through baryta water, insoluble barium carbonate is formed. Hence it is used in analytical chemistry as a "CO<sub>2</sub>-absorbent." Dried  $\text{Ba}(\text{OH})_2$  is used as a caustic.

**Barium Nitrate** [Ba(NO<sub>3</sub>)<sub>2</sub>].—This compound is formed by the action of nitric acid on the carbonate, hydroxide, or the sulfide of barium. It is found in Nature as *nitrobarite*. It crystallizes in the regular system, melts at 500° C., and has a specific gravity of 3.244 at  $\frac{23}{4}^{\circ}$ . One Gm. is soluble in 12 cc. of water at 15° C. and in 3.2 cc. of boiling water. It is used as a reagent (standardizing soap solution) for H<sub>2</sub>O analysis, etc. It is used in the manufacture of "green fire" and BaO<sub>2</sub>.

**Barium Oxide** ( $BaO$ ), Molecular Weight, 153.36. **Barium Dioxide** ( $BaO_2$ ), Molecular Weight, 169.36.—Like the other members of the alkaline earth group, barium forms a regular oxide and dioxide. Barium oxide (Barium Protoxide, Calcined Baryta) is made by heating the nitrate (1), or by heating the carbonate with powdered charcoal (2). The temperature at which barium carbonate may be calcined successfully is so high (above  $1500^{\circ} C.$ ) that the special method just indicated is employed.



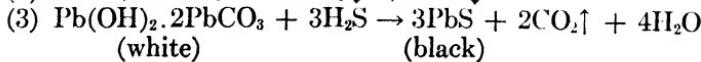
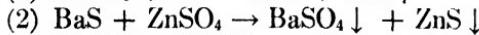
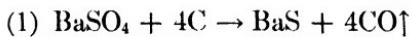
When barium monoxide is heated to redness in a current of air or oxygen, the dioxide is formed (3).



Barium dioxide (Barium Peroxide, Barium Superoxide) is only slightly soluble in water but combines with it to form the hydrate,  $\text{BaO}_2 \cdot 8\text{H}_2\text{O}$ . The hydrate is made by adding a solution of hydrogen peroxide to a solution of barium hydroxide (4). It is used in the manufacture of hydrogen peroxide (*q. v.*, p. 57), special glass, sugar, in oil refining, etc.



**Barium Sulfide** ( $\text{BaS}$ ).—Barium sulfide is made by reducing barium sulfate with carbon (1). This salt is used as a depilatory (in flour or starch paste) and in the manufacture of *lithopone*, a substance used in white or light colored paints. The latter is made by the double decomposition of barium sulfide and zinc sulfate (2) and, as a paint pigment, it has the distinct advantage over white lead by not being discolored by hydrogen sulfide (3).



# BERYLLIUM AND MAGNESIUM AND THEIR COMPOUNDS

**Introduction.**—Beryllium (synonym: *Glucinum*), magnesium, zinc, cadmium and mercury form Division B of Group II in Mendeléeff's Periodic Table. The elements of this family are bivalent. Mercury also acts univalently. The properties of these metals are not as similar as are those of the members of some other groups such as the alkaline earth metals, the alkali metals, etc. In a general way, beryllium chemically resembles aluminum and boron. It also resembles zinc but differs from magnesium in that its hydroxide is amphoteric, a property that might be anticipated because of its position between boron, a non-metal, and lithium, a metal. From a standpoint of chemical behavior and also of sulfate solubility, beryllium and magnesium more closely resemble zinc and cadmium than they do the alkali metals. On the other hand, beryllium and magnesium differ markedly from zinc and cadmium by not entering into complex ions and by not forming oxides reducible by carbon. Furthermore, beryllium and magnesium are light metals (density: Be-1.8; Mg-1.74) whereas zinc, cadmium and mercury are heavy metals (density: Zn-7.14; Cd-8.6; Hg-13.6). Unlike the alkali and alkaline earth hydroxides, the hydroxides of the metals of this group are nearly insoluble in water and are easily converted by heat into the metallic oxides and water. Mercury is the only member of this group that forms two series of compounds, *viz.*, mercurous (univalent mercury) and mercuric (bivalent mercury). In this respect, mercury resembles copper (Group I). The chemical activity of mercury places it between antimony and silver in the electro-motive series.

## CHAPTER XXI

### BERYLLIUM

Symbol, Be. Valence, II. Atomic Weight, 9.02; Atomic Number, 4

**History and Occurrence.**—Beryllium was discovered in 1797 by L. B. Vanquelin. It was isolated by Wöhler and Bussy in 1828 and obtained in pure form by Humpidge in 1885. It was named after the mineral *beryl*, from which it was obtained. The element is also called *glucinum* in allusion to the sweet taste of its salts. Although a somewhat rare metal, small quantities of it are found in quite a number of minerals. The widely distributed mineral known as *beryl*, a metasilicate of beryllium and aluminum [ $\text{Be}_3\text{Al}_2(\text{SiO}_4)_6$ ], is the principal source of this element. Beryls, containing a little chromium silicate, are known as *emeralds*. The mineral, *beryllonite*,

is a double phosphate of beryllium and sodium ( $\text{BeNaPO}_4$ ) and is found in Maine. It also occurs in *chrysoberyl* ( $\text{Be}(\text{AlO}_2)_2$ ), *phenakite* ( $\text{Be}_2\text{SiO}_4$ ), and in some other silicates.

**Physical and Chemical Properties.**—Beryllium is a hard, white, ductile and malleable metal. It is often obtained as hexagonal crystals. It has a specific gravity of 2.1 at 15° C., and a specific heat of 0.4079. At ordinary temperatures the metal is quite permanent in air or oxygen. When heated, it becomes coated with oxide ( $\text{BeO}$ ). It is soluble in dilute acids and, when heated with caustic alkalies, it forms beryllates with the evolution of hydrogen (1); a behavior similar to that of aluminum.



Beryllium combines readily with fluorine, chlorine and bromine.

**Commercial Manufacture.**—Beryl is crushed and fused with potassium carbonate. The cooled product is treated with sulfuric acid, diluted with water, and the silica filtered off. When this solution is concentrated, most of the aluminum separates as potassium alum. The mother liquor is treated with a hot, concentrated solution of ammonium carbonate which precipitates the iron and remaining aluminum, but keeps the beryllium in solution as a double carbonate. The precipitates of iron and aluminum are filtered off and, when the filtrate is boiled, beryllium hydroxide containing a little ferric oxide is thrown down. This hydroxide is then dissolved in ammonium carbonate and steam blown through the liquid to precipitate the oxide. This process is repeated several times and the final precipitate is dissolved in hydrochloric acid, concentrated and crystallized. The crystals of beryllium chloride are then fused and the metal separated by electrolysis. The metal may also be prepared by heating the chloride with sodium in an atmosphere of hydrogen.

**Compounds.**—Beryllium salts are usually obtained by dissolving either the oxide ( $\text{BeO}$ ) or the hydroxide ( $\text{Be(OH)}_2$ ) in the desired acids. These salts are hydrolyzed so readily that it is difficult to obtain a normal salt. Beryllium nitrate ( $\text{Be}(\text{NO}_3)_2$ ) may be prepared by dissolving beryllium hydroxide in nitric acid and crystallizing from the latter (not water). Beryllium sulfate ( $\text{BeSO}_4 \cdot 7\text{H}_2\text{O}$ ) is isomorphous with magnesium sulfate ( $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ ) and may be obtained by dissolving the oxide in sulfuric acid and crystallizing from acid solution. Like the hydroxides of aluminum and zinc, beryllium hydroxide (also oxide) is soluble in an excess of caustic alkalies and forms beryllates. Upon boiling or diluting their solutions, the hydroxide is reprecipitated.

**Pharmacological Action of Beryllium Ion.**—The action of beryllium sulfate was investigated by Seaman<sup>1</sup> in 1912. He observed that when this salt was administered orally to dogs, there resulted nutritional disturbances with loss of nitrogen, sulfur and phosphorus. In large doses, the salt was toxic. When injected intra-

<sup>1</sup> Biochem. Bull., 2, 184 (1912).

venously, this compound was especially toxic, disturbing the respiration, circulation and temperature. It was noted that it also inhibited the action of digestive ferments.

**Uses.**—Beryllium is never employed in medicine. Beryllium affects copper very much as carbon does iron. Because of the resonance possessed by beryllium-copper alloys, they are used to make wires for pianos and other musical instruments, artificial precious stones, and special electrical and scientific instruments.

## MAGNESIUM

Symbol, Mg. Valence, II. Atomic Weight, 24.32;  
Atomic Number, 12

**History and Occurrence.**—In 1695, N. Grew, a London physician, obtained magnesium sulfate by evaporating the water of a mineral spring at Epsom. This salt soon became celebrated for its medicinal properties and was called *Epsom Salt*. Magnesium oxide was not distinguished from calcium oxide until 1755, when J. Black showed them to be entirely different. The impure metal was first isolated by Davy in 1808. It is said that the element was named after Magnesia, a town in Asia Minor. A. B. Bussy<sup>1</sup> succeeded in preparing a quantity of fairly pure metal by treating the molten chloride with potassium. In 1852, Bunsen obtained magnesium metal by the electrolysis of the chloride and in 1857, H. Sainte Claire Deville devised a process for making it on a commercial scale.<sup>2</sup>

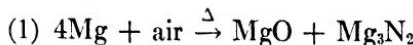
Magnesium is closely associated with calcium and occurs widely and abundantly distributed. As the free metal, it never occurs in Nature, and its compounds are not as plentiful as those of calcium. It is found chiefly in the forms of the silicate, carbonate and chloride. The principal silicates are *talc* [ $\text{Mg}_3\text{H}_2(\text{SiO}_3)_4$ ], *asbestos* [ $\text{CaMg}_3(\text{SiO}_3)_4$ ] and *meerschaum* [ $\text{Mg}_2\text{Si}_3\text{O}_8 \cdot 2\text{H}_2\text{O}$ ]. As the carbonate, it occurs in the mineral *magnesite* [ $\text{MgCO}_3$ ] and in large quantities as *dolomite* [ $\text{CaCO}_3 \cdot \text{MgCO}_3$ ] and *dolomitic limestone*. The Stassfurt deposits of *carnallite* [ $\text{KCl} \cdot \text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ ] have been referred to before (p. 222). Native magnesium sulfate [ $\text{MgSO}_4 \cdot \text{H}_2\text{O}$ ] is known as *kieserite*. Magnesium salts are associated with calcium compounds in plants. Magnesium phosphate occurs in bones and is one of the inorganic physiological constituents of urine.

**Physical Properties.**—Magnesium is a silver-white metal having a density of 1.74. The malleable and ductile properties of the metal permit it to be drawn into wire and then rolled into ribbons, in which form it comes into the trade. Magnesium alloys, *e. g.*, *magnalium* (aluminum containing about 2 per cent of magnesium) are light in weight, have a high tensile strength and take a brilliant polish. Magnesium melts at about 651° C. and boils at about 1380° C.

<sup>1</sup> J. d. pharm., 15, 30 (1829); 16, 142 (1830).

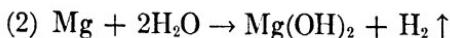
<sup>2</sup> Compt. rend. Soc. de biol. de Paris, 44, 394 (1857).

**Chemical Properties.**—Magnesium is permanent in dry air, but tarnishes in moist air. When heated in air, oxygen or even in carbon dioxide, it burns with a blinding white light that is rich in actinic rays of the violet and ultra-violet regions; hence its use in photography (1). "Flash-light" powders are mixtures of powdered magnesium and potassium chlorate or barium peroxide. This mixture is also used in pyrotechnics.



The metal will also burn in steam, carbon dioxide, sulfur vapors, sulfur dioxide, nitric oxide and nitrogen dioxide.

When burning magnesium is introduced into a current of steam, it decomposes the latter into hydrogen with the formation of magnesium hydroxide (2).



At high temperatures the metal acts as a reducing agent, reducing many metallic oxides to the metals, silica to silicon, and boron trioxide to boron.<sup>1</sup> When heated in an atmosphere of nitrogen, it forms the nitride ( $\text{Mg}_3\text{N}_2$ ) (see Nitrogen, p. 71). Magnesium occurs after calcium and before aluminum in the electromotive series of the metals (*q. v.*) and hence replaces many metals from solutions of their salts. The metal is readily soluble in acids with the evolution of hydrogen and the formation of salts. It is insoluble in alkalies. It never enters into complex ions.

The chemical reactions of interest that involve the magnesium ion are as follows: 1. Magnesium ion is precipitated by caustic alkalies (3).



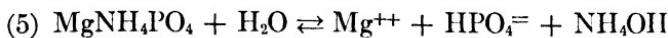
2. Ammonium hydroxide incompletely precipitates magnesium from solutions of magnesium salts. In the presence of an ammonium salt, ammonium hydroxide does not precipitate magnesium ion, because the concentration of the hydroxyl ion produced by the ammonium hydroxide is depressed by the excess of ammonium ions from the salt. Furthermore, when the concentration of magnesium ion is multiplied by the square of the concentration of the hydroxyl ion, there is obtained a product that is *less* than the ion-product constant of magnesium hydroxide and hence no precipitate will be formed.

3. When a solution of a magnesium salt is mixed with a solution of sodium phosphate containing an equal volume of a solution of ammonium chloride and a little ammonia water, a white crystalline precipitate of magnesium ammonium phosphate is produced (4).

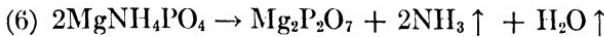


<sup>1</sup> Moissan: Compt. rend. Soc. de biol. de Paris, 114, 392 (1892).

The presence of ammonium chloride prevents the precipitation of magnesium hydroxide (3) and the ammonium hydroxide lessens the hydrolysis (5) and decreases the solubility of the salt.



By ignition, magnesium ammonium phosphate is converted into the pyrophosphate (6).



4. The dyes, para-nitrobenzene-azo-resorcinol,<sup>1</sup>  $\text{NO}_2\text{C}_6\text{H}_4\text{N}=\text{N}-\text{C}_6\text{H}_3(\text{OH})_2$  and para-nitrobenzene-azo- $\alpha$ -naphthol,  $\text{NO}_2\text{C}_6\text{H}_4\text{N}=\text{N.C}_{10}\text{H}_7\text{OH}$ , in a concentration of 0.5 per cent in a 1 per cent solution of sodium hydroxide will detect  $\frac{1}{300}$  mg. of magnesium. The solution to be tested is made slightly acid with dilute hydrochloric acid and then 1 drop of the reagent is added. When the solution is made alkaline with dilute sodium hydroxide, a characteristic sky-blue insoluble magnesium lake is formed. When the amount of magnesium is very small, the dilution of the stock solution with four or five times its volume of water seems to increase the sensitivity of the test. Shaking for two or three minutes serves to coagulate the slowly forming lake.

Traces of calcium and barium likely to be present in the course of the regular analysis should be removed by the addition of ammonium sulfate and oxalate. It has been found that an excess of ammonium salts cuts down the sensitivity of the reagent, so they should be volatilized by ignition in a casserole before the test is made.

Somewhat similar blue lakes are formed with both nickel and cobalt, so care should be taken to completely eliminate these elements.

**Commercial Manufacture.**—Magnesium metal is obtained by the electrolysis of fused magnesium chloride. The source of magnesium chloride is from (1) underground brines and (2) sea water.

1. Underground brines contain among other salts about 3 per cent of magnesium chloride. This is obtained by evaporation and fractional crystallization as the double salt,  $2\text{MgCl}_2 \cdot \text{CaCl}_2 \cdot 12\text{H}_2\text{O}$ . The double salt is then treated to yield  $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ . Anhydrous magnesium chloride suitable for electrolysis is obtained by heating.

2. Sea water has become an important source of magnesium since about 1940. It contains about 0.5 per cent  $\text{MgCl}_2$ . The magnesium is precipitated as the hydroxide by alkali. Hydrochloric acid is then added to form the magnesium chloride which is removed by crystallization and made anhydrous by heating.

The electrolysis is carried out in quite a normal manner at the fusion point of magnesium chloride (about  $750^\circ \text{C.}$ ). The chlorine is removed at the anode and molten magnesium rises to the top and is skimmed off.

<sup>1</sup> Ruigh: J. Am. Chem. Soc., 51, 1456 (1929).

**Pharmacological Action of Magnesium Ion.**—The magnesium ion is essential to life in the human body. It is present in blood plasma to the extent of about 3 mg. per 100 cc. It is apparently indispensable to the smooth functioning of the neuromuscular system.

Meltzer<sup>1,2</sup> pointed out that magnesium salts when injected intramuscularly or intravenously have a powerful anesthetic action which resembles that produced by chloroform.

Magnesium ion is not readily absorbed from the gastro-intestinal tract as its absorption is retarded by alkaline media and increased by acid media. Most of the absorption takes place in the acid media of the duodenum.

Investigations by A. D. Hirschfelder and V. G. Haury<sup>3</sup> have shown that normal men excrete *via* the urine, 40 to 44 per cent of the magnesium taken in a single purgative dose of Epsom salt within twenty-four hours. However, the concentration of magnesium in the blood plasma (normal average, 3 mg. per 100 cc.) was raised only slightly, the average increase being 0.24 mg. per 100 cc. In the presence of kidney deficiency in both animals and men, it was found that a single purgative dose of Epsom salt was able to increase the magnesium level to two-thirds of the coma level, which is 17 mg. per 100 cc. of plasma.

**Uses.**—Magnesium alloys are fast becoming structural metals because of their rigidity and lightness. Magnesium is used in pyrotechnics and photography and is a constituent of alloys and is employed in making magnesium salts.

## OFFICIAL MAGNESIUM COMPOUNDS

### MAGNESIUM CARBONATE

*Magnesium Carbonate*, U. S. P. XIII

Approximate Formula,  $(\text{MgCO}_3)_4 \cdot \text{Mg}(\text{OH})_2 \cdot 5\text{H}_2\text{O}$   
Molecular Weight, 485.74

**Physical Properties.**—Magnesium carbonate is a white, bulky, odorless powder having a slightly "earthy" taste. It often occurs in light, white, friable masses. It is stable in air.

The salt is nearly insoluble in water, to which it imparts a slightly alkaline reaction which is due, no doubt, to a slight dissociation of  $\text{Mg}(\text{OH})_2$ . It is insoluble in alcohol but dissolves with effervescence in dilute acids.

**Chemical Properties.**—Magnesium carbonate is insoluble in most solvents and thus is quite inert chemically. Dilute acids dissolve it with effervescence. An acid solution gives the tests for the magnesium ion (*q. v.*).

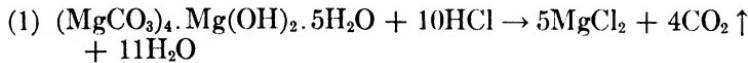
<sup>1</sup> Am. J. Physiol., vols. 14, 366 (1905); 23, 141, (1908-9).

<sup>2</sup> J. Pharmacol., 1, 1 (1909).

<sup>3</sup> J. Am. Med. Assn., 102, 1138 (1935).

**Official Tests for Identity.**—1. When magnesium carbonate is treated with dilute hydrochloric acid, it dissolves with the evolution of carbon dioxide (1).

2. The solution obtained in (1) responds to the tests for magnesium ion.

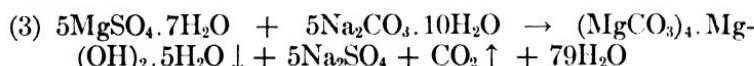


(a) If to the solution is added ammonium chloride and then ammonium carbonate T.S., no precipitate forms.

(b) A white precipitate is produced when ammonium chloride and sodium phosphate T.S. are added to a solution containing magnesium ions (2).



**Commercial Manufacture.**—When solutions of sodium carbonate and magnesium sulfate are mixed, a precipitate of basic magnesium carbonate is formed. The composition of this basic salt varies according to the concentrations and temperatures of the solutions of the reacting substances and also according to the temperatures at which the precipitate is dried. Thus, when cold dilute solutions of sodium carbonate and magnesium sulfate are mixed, no carbon dioxide is evolved, a very bulky, white precipitate of basic carbonate is thrown down and an appreciable amount of magnesium bicarbonate [ $\text{Mg(HCO}_3)_2$ , soluble] remains in solution. This can be precipitated as basic carbonate by boiling. When hot, concentrated solutions of the reacting substances are mixed, carbon dioxide is given off and a salt containing a greater proportion of magnesium hydroxide is obtained. Consistent with the ease of manufacture, bulkiness of product, etc., a process has been devised whereby an aqueous solution of magnesium sulfate (125 Gm. per liter) is mixed with an aqueous solution of sodium carbonate (150 Gm. per liter), the temperature of the solutions not exceeding 55° C. The resulting precipitate is washed to remove sodium sulfate and dried without heat. The following equation approximately represents the metathesis (3).

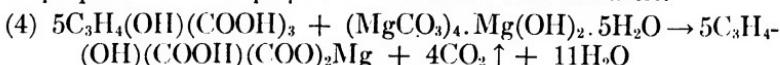


**Pharmaceutical Preparations and Uses.**—1. *Magnesium Carbonate* (*Magnesii Carbonas*, *Magnesia Alba*), U. S. P. XIII.—Magnesium Carbonate is a basic hydrated magnesium carbonate or a normal hydrated magnesium carbonate. It contains the equivalent of not less than 40 per cent and not more than 43.5 per cent of MgO.

Official magnesium carbonate is used as an antacid and laxative. It is contraindicated only when the stomach must not be burdened with carbon dioxide. In the alimentary tract, this basic salt is

converted into soluble magnesium bicarbonate and, therefore, acts as a laxative. Soluble salts of magnesium act as cathartics because (salt action) they are reduced in the intestines to isotonic conditions by the absorption of liquid. This liquid, together with the salts, is retained in the intestines, increases the quantity and fluidity of the intestinal contents and mechanically stimulates peristalsis. In preparations that are alkaline, magnesium carbonate may be used as a clarifying or filtering agent. It is also used as an abrasive in some tooth powders, as a cosmetic, and as an ingredient in silver polishes. Average dose—Antacoid, 0.6 Gm. (approximately 10 grains)—Laxative, 8 Gm. (approximately 2 drachms).

2. *Magnesium Citrate Solution* (*Liquor Magnesii Citratis*), U. S. P. XIII.—Magnesium Citrate Solution contains, in each 100 cc., an amount of magnesium citrate corresponding to not less than 1.6 Gm. and not more than 1.9 Gm. of MgO. A suspension of magnesium carbonate in distilled water is added to a hot aqueous solution of citric acid and the mixture stirred until solution is effected (4). Syrup is added and the solution heated to the boiling-point. Purified talc, with which oil of lemon has been triturated, is added and the mixture filtered while hot into a strong bottle that has been rinsed with boiling water. Sufficient boiled distilled water is then added to bring the volume up to 350 cc. The bottle is stoppered with a peldorf of purified cotton and after the contents have cooled, the potassium bicarbonate is introduced and the bottle immediately stoppered. The bottle is shaken occasionally to facilitate solution of the bicarbonate (5). It is recommended that the bottle be kept on its side in a cool place, preferably in a refrigerator. The excess of citric acid reacts with the potassium bicarbonate to form potassium citrate and carbon dioxide. The latter charges the solution and makes it more palatable. An equivalent amount of sodium bicarbonate, preferably in tablet form, may be used in place of the potassium bicarbonate. The stability of this solution is improved by adjusting the quantity of magnesium carbonate for each 350 cc. of solution so that it corresponds to 6 Gm. of MgO and by sterilizing the solution after it has been bottled. This preparation is employed as a laxative and cathartic.



Recently<sup>1</sup> there has been developed a very stable form of neutral magnesium carbonate,  $\text{MgCO}_3 \cdot \text{H}_2\text{O}$ . This has been used in preparing a dry powder mixture of the U. S. P. formula for citrate of magnesia. The official solution can be made by simple solution. Average dose—200 cc. (approximately 7 fluidounces).

3. *Tolu Balsam Syrup* (*Syrupus Balsami Tolutani*, Syrup of Tolu), U. S. P. XIII.—Magnesium carbonate acts as an excellent clarifying agent and, because of its slight alkalinity, it also assists

<sup>1</sup> J. Am. Pharm. Assn., Pr. Ed., 2, 213 (1941).

in effecting the solution of the resinous constituents of the tolu. This syrup is a very mild expectorant, although it is more often used as a pleasant vehicle. Average dose—2 cc. (approximately 30 minimis).

4. *Carminative Mixture* (*Mistura Carminativa*, *Dalby's Carminative*), N. F. VIII.—It contains, in addition to the other ingredients, 65 Gm. of Magnesium Carbonate in each 1000 cc. of the mixture.

The magnesium carbonate contributes to the antacid properties. Average dose—For infants, 0.5 cc. (approximately 8 minimis).

5. *Aromatic Eriodictyon Syrup* (*Syrupus Eriodictyi Aromaticus*, *Aromatic Yerba Santa Syrup*, *Syrupus Corrigens*), N. F. VIII.—Magnesium carbonate is used primarily as a clarifying agent but its slight alkalinity assists in the solution of the resins. The preparation is used as a masking vehicle for bitter medicines. (See Potassium Hydroxide, p. 246.) Average dose—8 cc. (approximately 2 fluidrachms).

6. *Ginger Syrup* (*Syrupus Zingiberis*), N. F. VIII.—Magnesium carbonate acts as a dispersing and clarifying agent besides imparting a slight alkalinity to the syrup.

7. *Thyme Syrup* (*Syrupus Thymi*), N. F. VIII.—The slight alkalinity imparted to the syrup by the magnesium carbonate assists in keeping the resins of the thyme in solution.

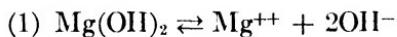
## MAGNESIUM HYDROXIDE

### *Magnesium Hydroxide*, N. F. VIII

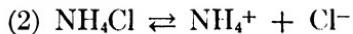
Formula,  $\text{Mg}(\text{OH})_2$ . Molecular Weight, 58.34

**Physical Properties.**—Magnesium hydroxide occurs as a bulky white powder. It is practically insoluble in water and in alcohol but soluble in dilute acids.

**Chemical Properties.**—A solution of magnesium hydroxide is faintly alkaline. Sodium hydroxide or potassium hydroxide reduce the solubility of magnesium hydroxide, whereas the addition of ammonia or ammonium chloride increases it. Magnesium hydroxide in aqueous solution ionizes into magnesium ions and hydroxyl ions (1).



The addition of ammonium chloride provides a supply of ammonium ions (2).



The ammonium ions combine with the hydroxyl ions (equation 1) to form practically non-ionized ammonium hydroxide. This causes the reaction represented in (1) to proceed to the right and results in more magnesium hydroxide going into solution. This process goes on until the solubility product of magnesium hydroxide is reached. (See *Magnesia Mixture T.S.*, U. S. P. XIII, p. 839).

Like many hydroxides, that of magnesium will readily absorb carbon dioxide. A novel use of magnesium hydroxide is its incorporation into cheese before canning as a carbon dioxide absorbent.<sup>1</sup>

Magnesium hydroxide when dissolved in an acidic solution will respond to the reactions of the magnesium ion (see p. 354).

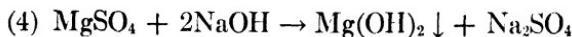
**Official Tests for Identity.**—1. A solution of magnesium hydroxide (1 in 20) in diluted hydrochloric acid responds to the tests for magnesium. (See Magnesium Carbonate, p. 357.)

**Commercial Manufacture.**—Most of the magnesium hydroxide is prepared by the hydration of magnesium oxide (3).



The hydroxide is collected and washed on a filter and dried.

It is also prepared by mixing a solution of magnesium sulfate and sodium hydroxide (4).



This method has the disadvantage of having a long and tedious washing process to remove the sodium sulfate.

**Pharmaceutical Preparations and Uses.**—1. *Magnesium Hydroxide* (*Magnesii Hydroxidum*), N. F. VIII.—Magnesium Hydroxide contains not less than 95 per cent of  $\text{Mg(OH)}_2$ . Due to its basic character it is an efficient antacid and the magnesium chloride formed in the stomach exerts a “salt action” in the intestinal tract (see Magnesium Carbonate, p. 358), causing a mild laxative action. Average dose—0.3 Gm. (approximately 5 grains).

2. *Magnesium Hydroxide Tablets* (*Tabellæ Magnesii Hydroxidi*, “Milk of Magnesia Tablets”), N. F. VIII.—Magnesium Hydroxide Tablets contain not less than 93 per cent and not more than 107 per cent of the labeled amount of  $\text{Mg(OH)}_2$ , the amount being expressed by weight. Average dose—0.3 Gm. (approximately 5 grains).

3. *Magnesia Magma* (*Magma Magnesiae*, Milk of Magnesia), U. S. P. XIII.—Magnesia Magma is a suspension of magnesium hydroxide containing not less than 7 per cent and not more than 8.5 per cent of  $\text{Mg(OH)}_2$ . For purposes of minimizing the action of the glass container on Magnesia Magma, 0.1 per cent of citric acid may be added. Most Milk of Magnesia is prepared by the hydration of magnesium oxide (3). It was prepared by the old method of double-decomposition by slowly adding a solution of sodium hydroxide to a boiling solution of magnesium sulfate (4). The mixture was boiled for thirty minutes and then mixed with hot distilled water in a cylindrical vessel. When the precipitate had settled, the supernatant liquid was decanted and the magma again washed with hot distilled water. The washing was repeated until the liquid failed to give a test for sulfate ion. The mixture was concentrated by evaporation until it contained the required amount of  $\text{Mg(OH)}_2$ . One-half cc. of a volatile oil or a blend of volatile

<sup>1</sup> Aminco Lab. News (March 1947).

oils, suitable for flavoring purposes, were usually added to each 1000 cc. of Magnesia Magma. It should be stored at temperatures not exceeding 35° C., and should not be permitted to freeze. Average dose—Antacid, 4 cc. (approximately 1 fluidrachm); Laxative, 15 cc. (approximately 4 fluidrachms.)

### MAGNESIUM OXIDE

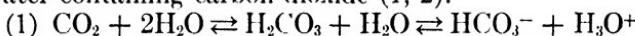
*Magnesium Oxide*, U. S. P. XIII

*Heavy Magnesium Oxide*, U. S. P. XIII

Formula, MgO. Molecular Weight, 40.32

**Physical Properties.**—Magnesium Oxide usually occurs as a very bulky, white powder but it may be moulded into cubes. The heavy magnesium oxide occurs as a relatively dense, white powder. Both are odorless, insoluble in water and alcohol but soluble in dilute acids. The two oxides differ from one another in density; the bulk of a definite weight of light magnesium oxide being about three and a half times that of the same weight of heavy magnesium oxide.

**Chemical Properties.**—Upon exposure to air, they absorb carbon dioxide and moisture. Light magnesium oxide hydrolyzes to  $\text{Mg}(\text{OH})_2$  more easily than the heavy oxide and will dissolve readily in water containing carbon dioxide (1, 2).



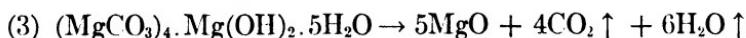
When the light oxide is finely ground and mixed with a solution of magnesium chloride the mass sets to a hard, strong and durable cement. The composition is thought to be  $3\text{MgO} \cdot \text{MgCl}_2 \cdot 10\text{H}_2\text{O}$ , although some  $\text{Mg}(\text{OH})_2$  could also be present. A mixture of this type is known as magnesia cement, oxychloride cement, Sorel's cement, or zylolith.

Magnesium oxide fuses at about 2800° C. and at such high temperatures is reduced by carbon, forming magnesium carbide.

A solution of magnesium oxide in dilute acid responds to the reactions of the magnesium ion (see p. 354).

**Official Test for Identity.**—When the oxides are converted into magnesium chloride by treatment with hydrochloric acid, the resulting solution responds to all tests for *Magnesium* ion (*q. v.*).

**Commercial Manufacture.**—*Light Magnesium Oxide.*—This form of magnesium oxide is made by firmly pressing official magnesium carbonate into a crucible and heating to *dull redness* (3) until a small test-sample no longer effervesces with hydrochloric acid.



**Heavy Magnesium Oxide.**—A heavy oxide may be obtained by heating to *white heat* official magnesium carbonate that has been firmly packed in a crucible. Magnesium oxide of greatest com-

pactness is obtained by heating to redness the washed and dried magnesium carbonate (heavy) that is obtained by mixing boiling aqueous solutions of magnesium sulfate and sodium carbonate.

**Pharmaceutical Preparations and Uses.**—1. *Magnesium Oxide* (*Magnesii Oxidum*, *Magnesia*, *Light Magnesia*), U. S. P. XIII.—Magnesium Oxide contains, after ignition, not less than 96 per cent of MgO. It is used as an antacid and laxative. Average dose—Antacid, 0.25 Gm. (approximately 4 grains); Laxative, 4 Gm. (approximately 60 grains).

2. *Heavy Magnesium Oxide* (*Magnesii Oxidum Ponderosum*, *Heavy Magnesia*), U. S. P. XIII.—Heavy magnesium has the same purity rubric, use and dose as magnesium oxide.

3. *Aromatic Cascara Sagrada Fluidextract* (*Fluidextractum Cascarae Sagradæ Aromaticum*), U. S. P. XIII.—As has been previously pointed out, magnesium oxide unites slowly with water to form the sparingly soluble magnesium hydroxide, which gives the solution a faintly alkaline reaction. Magnesium oxide (with some magnesium hydroxide) is allowed to react for forty-eight hours with the bitter principles of the cascara bark. This mitigates the bitterness of the finished preparation. It is used as a laxative. Average dose—2 cc. (approximately 30 minimis).

4. *Hydrastis Extract* (*Extractum Hydrastis*, *Goldenseal Extract*, *Powdered Hydrastis Extract*), N. F. VIII.—Because magnesium oxide can absorb moisture and thus maintain a dry condition around it, the oxide, together with starch, is used in this preparation as a diluent. Average dose—0.5 Gm. (approximately 7½ grains).

5. *Compound Rhubarb Powder* (*Pulvis Rhei Compositus*, *Gregory's Powder*), N. F. VIII.—This powder contains 65 per cent of magnesium oxide, together with powdered rhubarb and powdered ginger. Magnesium oxide neutralizes the tannic acid in the rhubarb and thus reduces the astringent property. The powder is used as an antacid and laxative. Average dose—2 Gm. (approximately 30 grains).

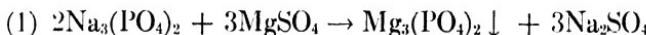
6. *Sodium Bicarbonate and Magnesium Oxide Powder* (*Pulvis Sodii Bicarbonatis et Magnesii Oxidi*, *Sippy Powder No. 2*), N. F. VIII.—This powder "contains not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of NaHCO<sub>3</sub>, and not less than 90 per cent and not more than 110 per cent of the labeled amount of MgO." The powder contains 50 per cent of each ingredient. It is used as an antacid, particularly in the treatment of stomach ulcers. Average dose—1.3 Gm. (approximately 20 grains).

7. *Sodium Bicarbonate and Magnesium Oxide Tablets* (*Tabellæ Sodii Bicarbonatis et Magnesii Oxidi*, *Sippy Powder Tablets No. 2*), N. F. VIII.—These tablets have the same purity rubric, use and dose as the powder.

**TRIBASIC MAGNESIUM PHOSPHATE***Tribasic Magnesium Phosphate*, N. F. VIIIFormula,  $Mg_3(PO_4)_2 \cdot 5H_2O$ . Molecular Weight, 353.00

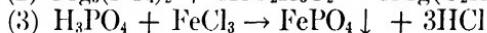
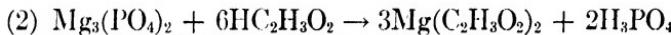
**Physical Properties.**—Tribasic Magnesium Phosphate is a white, odorless, and tasteless powder. It is almost insoluble in water but is readily soluble in diluted mineral acids.

**Chemical Properties.**—Tribasic magnesium phosphate is readily precipitated from solutions of magnesium salts with trisodium phosphate (1).



Ordinary sodium phosphate,  $Na_2HPO_4$ , slowly precipitates magnesium hydrogen phosphate,  $MgHPO_4 \cdot 7H_2O$ , soluble in 322 parts of cold water. When the salt is dissolved in diluted nitric or hydrochloric acid it responds to the tests for the magnesium ion (see p. 354). A dilute nitric acid solution of the salt will give a yellow precipitate of ammonium phosphomolybdate with ammonium molybdate T.S. (see p. 128).

The phosphate ion may be removed by dissolving tribasic magnesium phosphate in diluted acetic acid and adding a solution of ferric chloride T.S. (2, 3).



The solution thus obtained by filtering out the white ferric phosphate will respond to all the tests for the magnesium ion.

**Official Tests for Identity.**—1. Ammonium molybdate T.S. added to a solution of Tribasic Magnesium Phosphate in diluted nitric acid produces a precipitate of yellow ammonium phosphomolybdate which is soluble in ammonia T.S.

2. Dissolve 0.1 Gm. of tribasic magnesium phosphate in 0.7 cc. of diluted acetic acid and 20 cc. of distilled water. Add 1 cc. of ferric chloride T.S., let stand five minutes and filter. Five cc. of the filtrate responds to the test for magnesium (*q. v.*).

**Commercial Manufacture.**—When a solution of trisodium orthophosphate is added to a solution of magnesium sulfate, magnesium triphosphate is precipitated (1). The precipitate is washed with water until free from sodium sulfate and dried.

**Pharmaceutical Preparations and Uses.**—1. *Tribasic Magnesium Phosphate* (*Magnesii Phosphas Tribasicus*), N. F. VIII.—Tribasic Magnesium Phosphate, when ignited to constant weight, contains not less than 98 per cent of  $Mg_3(PO_4)_2$ . This insoluble compound is used quite extensively as an antacid. When so used, an amount sufficient only to neutralize excess acid in the stomach is rendered soluble and, therefore, it does not produce systemic alkalization as do magnesium hydroxide, sodium bicarbonate, etc. The antacid

action is accounted for by the fact that the phosphate ion ( $\text{PO}_4^{3-}$ ) will not exist as such in a medium containing hydronium ions ( $\text{H}_3\text{O}^+$ ). The  $\text{H}_3\text{O}^+$  combines with  $\text{PO}_4^{3-}$  to form relatively non-ionized  $\text{HPO}_4^{2-}$ , thus reducing the  $\text{H}_3\text{O}^+$  concentration in the stomach. A mild laxative action has been attributed to tribasic magnesium phosphate. Average dose—1 Gm. (approximately 15 grains).

**2. Tribasic Magnesium Phosphate Tablets** (*Tabellae Magnesii Phosphatis Tribasici*), N. F. VIII.—These tablets contain not less than 93 per cent and not more than 107 per cent of the labeled amount of  $\text{Mg}_3(\text{PO}_4)_2 \cdot 5\text{H}_2\text{O}$ . Average dose—1 Gm. (approximately 15 grains).

### MAGNESIUM SULFATE

#### *Magnesium Sulfate*, U. S. P. XIII

Formula,  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ . Molecular Weight, 246.49

**Physical Properties.**—This form of magnesium sulfate occurs in small, colorless, prismatic needles or rhombic prisms that are odorless and have a bitter, cooling, saline taste.

One Gm. of Magnesium Sulfate dissolves in 1 cc. of water and slowly in about 1 cc. of glycerin, at  $25^\circ \text{ C}$ . One Gm. dissolves in 0.2 cc. of boiling water. It is sparingly soluble in alcohol at  $25^\circ \text{ C}$ .

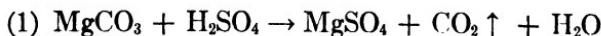
The salt is efflorescent. When gently heated, it readily loses some of its water of hydration and is converted into the monohydrate (a white powder) which quickly becomes anhydrous at  $200^\circ \text{ C}$ .

Magnesium sulfate crystallizes from cold water in the form of rhombic prisms or in needles of the heptahydrate ( $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ ). It is known as Epsom salt. With many other sulfates, magnesium sulfate forms double salts that are isomorphous with one another and also with analogous salts of zinc. They have a general formula  $\text{M}_2\text{SO}_4 \cdot \text{MgSO}_4 \cdot 6\text{H}_2\text{O}$ , where M represents potassium, sodium, ammonium, etc.

**Chemical Properties.**—An aqueous solution of magnesium sulfate is neutral to litmus paper. Aqueous solutions of the salt respond to the chemical reactions of the magnesium ion (*q. v.*) and the sulfate ion (see p. 212).

**Official Tests for Identity.**—Aqueous solutions of the salt respond to all tests for the *Magnesium* ion (*q. v.*) and for the *Sulfate ion*. (See Sodium Sulfate, p. 212.)

**Commercial Manufacture.**—1. Magnesium sulfate is made by treating native magnesium carbonate (magnesite) with sulfuric acid (1). The evolved carbon dioxide is usually used for "carbonating" waters. The residue is dissolved in hot water, the excess of sulfuric acid neutralized with magnesite, and barium sulfide added to precipitate any iron that may be present as soluble sulfate. The clear supernatant liquid is drawn off, concentrated and allowed to crystallize.



2. Large quantities of magnesium sulfate are obtained from *okieserite* ( $MgSO_4 \cdot H_2O$ ), a native form of the salt. This mineral is only sparingly soluble in cold water and therefore must be heated to change it to the soluble anhydrous salt. When the solution is concentrated and allowed to cool, crystals of the heptahydrate ( $MgSO_4 \cdot 7H_2O$ ) separate out. The product may be purified by recrystallization from water.

**Pharmaceutical Preparations and Uses.**—1. *Magnesium Sulfate* (*Magnesii Sulfas*, Epsom Salt), U. S. P. XIII.—Magnesium Sulfate, when rendered anhydrous by ignition, contains not less than 99.5 per cent of  $MgSO_4$ . It contains not less than 40 per cent and not more than 52 per cent of water.

This salt is very widely used as a saline cathartic. Since both the sulfate and magnesium ions are not readily absorbed, the cathartic action is perhaps due to the irritant action of these ions on the bowel and to an increase in flow of the intestinal juices. The "salt action" resulting in an osmotic retention of fluid in the intestine is also a means of explaining the cathartic property. (See Magnesium Carbonate, p. 358.) Average dose—15 Gm. (approximately 4 drachms).

2. *Magnesium Sulfate Ampuls* (Ampullæ Magnesii Sulfatis, Magnesium Sulfate Injection), N. F. VIII.—These ampuls contain a sterile solution of magnesium sulfate in water for injection and yield anhydrous magnesium sulfate,  $MgSO_4$ , equal to not less than 46 per cent and not more than 53 per cent of the labeled amount of magnesium sulfate,  $MgSO_4 \cdot 7H_2O$ . Average dose—1 Gm.

### MAGNESIUM TRISILICATE

#### *Magnesium Trisilicate*, U. S. P. XIII

Formula,  $2MgO \cdot 3SiO_2 \cdot nH_2O$

**Physical Properties.**—Magnesium Trisilicate is a fine, white, odorless, tasteless powder, free from grittiness. It is almost insoluble in water and in alcohol.

**Chemical Properties.**—Magnesium trisilicate when treated with diluted sulfuric acid decomposes to form magnesium sulfate and a residue of silicon dioxide (1).



In the stomach a similar reaction takes place with hydrochloric acid and a gelatinous mass is formed with the gastric contents.

**Official Tests for Identity.**—1. Mix about 0.5 Gm. of Magnesium Trisilicate with 10 cc. of diluted hydrochloric acid, filter, and neutralize the filtrate to litmus paper with ammonia T.S.; the neutralized filtrate responds to the tests for *Magnesium ion* (p. 357).

2. Prepare a bead by fusing a few crystals of sodium ammonium phosphate on a platinum loop in the flame of a Bunsen burner.

Place the hot, transparent bead in contact with Magnesium Trisilicate, and again fuse. Silica floats about in the bead, producing, upon cooling, an opaque bead with a web-like structure.

**Methods of Manufacture.**—In general, Magnesium Trisilicate is prepared by slowly running a solution of magnesium sulfate into a solution of sodium silicate. The precipitate is washed, dried, and powdered. It may also be prepared by adding an amount of hydrochloric acid to the sodium silicate solution and then adding cream of magnesia or precipitated magnesium hydroxide. Instant granulation takes place throughout the whole mass. No silica will be precipitated immediately upon the addition of hydrochloric acid to the sodium silicate solution provided the solutions are well diluted. The granular material is washed, dried, and powdered.<sup>1</sup>

**Pharmaceutical Preparations and Uses.**—1. *Magnesium Trisilicate* (Magnesii Trisilicas), U. S. P. XIII.—This is a compound of magnesium oxide and silicon dioxide with varying proportions of water. It contains not less than 20 per cent of magnesium oxide ( $MgO$ ) and not less than 45 per cent of silicon dioxide ( $SiO_2$ ). This magnesium salt of meso-(deutro-) trisilicic acid is used to relieve gastric hyperacidity and pain in gastric and duodenal ulcer. Its action is chemical but it does not interfere with peptic digestion nor does it induce systemic alkalization. In normal amounts it is non-toxic and it possesses adsorptive properties. In large doses it sometimes induces diarrhea because of the magnesium chloride formed with the hydrochloric acid in the stomach. The silicon dioxide which is formed and hydrated in the stomach passes into the intestine and there functions as an absorbent. This absorbent property makes magnesium trisilicate more than just a good antacid. In the stomach a gelatinous mass is formed that is protective to ulcers and prolongs the antacid properties for several hours. One Gm. of magnesium trisilicate can neutralize about 155 cc. of 0.1 N hydrochloric acid. Since it is insoluble in neutral and basic solutions, the antacid action stops in the stomach when all the hydrochloric acid is neutralized and thus prevents the development of an alkaline condition.

Magnesium trisilicate powder is an emulsifying agent for mineral, vegetable and animal oils when used in the proper proportions. An oil-in-water emulsion is produced which is probably brought about by mechanical action.<sup>2</sup> Average dose—1 Gm. (approximately 15 grains).

2. *Magnesium Trisilicate Tablets* (Tabellæ Magnesii Trisilicatis), U. S. P. XIII.—Average dose—1 Gm. (approximately 15 grains).

## ASBESTOS

The name *asbestos* has been given to certain minerals that are fibrous in character and are poor conductors of heat. The best

<sup>1</sup> Glass, Norman: Quart. J. Pharm. and Pharmacol., 9, 445 (1936).

<sup>2</sup> J. Am. Pharm. Assn., Pr. Ed., 7, 123 (1946).

known minerals that have asbestosiform varieties are: *Serpentine* [ $\text{H}_4\text{Mg}_3\text{Si}_2\text{O}_6$ ], *amphibole* [ $\text{Ca}(\text{Mg}, \text{Fe})_3\text{Si}_4\text{O}_{12}$ ], *anthophyllite* [ $(\text{Mg}, \text{Fe})\text{SiO}_3$ ], and *tremolite* [ $\text{CaMg}_3\text{Si}_4\text{O}_{12}$ ]. The best quality, long-fiber asbestos is found in veinlets in serpentine. It is thought to have been formed by the alteration of peridotite and other rocks by water.

The most important deposits of asbestos are found in a belt of igneous rock, that extends about 250 miles northeastward from northern Vermont into Canada, in Russia, Cape of Good Hope, and in Wyoming and Arizona.

The asbestos is usually mined along with the waste rock. The material is crushed and separated by means of an air blast which blows the lighter asbestos from the heavier rock.

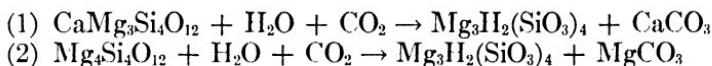
Asbestos is purified by boiling it for one hour with dilute hydrochloric acid and then washing it free from acid. Because it is not affected by fire, it is used as a filtering medium for those substances that are to be subjected to high temperatures. The lower grades of asbestos are mixed with cement and made into fire-proof shingles and boards. Fire-proof plaster is made by incorporating asbestos in ordinary wall plaster.

### TALC

#### *Talc*, U. S. P. XIII

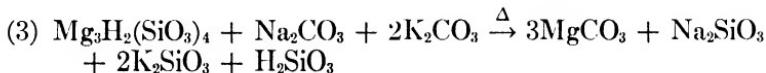
**Physical Properties.**—Talc is a very fine white or grayish-white, crystalline powder. It is unctuous, adhering readily to the skin, and is free from grittiness.

**Chemical Properties.**—Talc is formed by the breaking down of tremolite, instatite and other magnesian minerals. According to Clark,<sup>1</sup> the reactions may be represented as follows:



Soapstone is a dense and impure form of talc. Talc is an inert substance showing little activity to acids or bases. Upon fusion with sodium and potassium carbonate, the magnesium is removed in a soluble form while the silicon remains as an insoluble oxide.

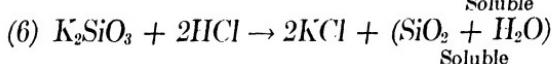
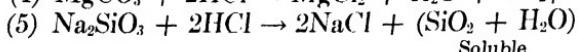
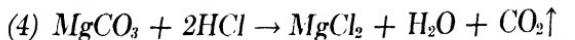
**Official Tests for Identity.**—Mix 500 mg. of Talc with 200 mg. of anhydrous sodium carbonate and 2 Gm. of anhydrous potassium carbonate, and heat the mixture in a platinum crucible until fusion is complete (3).



Cool, and transfer the fused mixture to a dish or beaker with the aid of about 50 cc. of hot water. Add hydrochloric acid to the

<sup>1</sup> Clark, F. W.: The Data of Geochemistry, 3d ed., U. S. Geol. Survey Bull., 616, 415 (1916).

liquid until it ceases to cause effervescence, then add 10 cc. more of the acid (4, 5, 6),



Soluble  
Soluble

and evaporate the mixture to dryness on a water-bath. The silicic acid formed by the reactions expressed in equations 5 and 6,  $\text{H}_2\text{SiO}_3$  ( $\text{SiO}_2 + \text{H}_2\text{O}$ ), when heated to 100° C. loses all but 13 per cent of its water and the silica becomes insoluble. Cool, add 20 cc. of water, boil, and filter the mixture. An insoluble residue of silica remains. The filtrate contains soluble magnesium chloride and responds to the tests for magnesium ion (*q. v.*).

**Commercial Manufacture.**—Purified talc is made by boiling very finely powdered talc with water containing about 2 per cent of hydrochloric acid, allowing the insoluble matter to subside, decanting the supernatant liquid and repeating the process with a weaker hydrochloric acid. The talc that has been freed of iron and other soluble impurities is thoroughly washed with water and dried at 110° C.

**Pharmaceutical Preparations and Uses.**—*Talc* (Talcum, Purified Talc, U. S. P. XII), U. S. P. XIII.—“Talc is a native, hydrous magnesium silicate, sometimes containing a small proportion of aluminum silicate.”

Because of its insolubility, it is employed as a filtering medium. For such use it should not be finer than the powder which passes through a No. 80 sieve but is retained by a No. 100 sieve. A powder finer than No. 100 is not retained by the average filter paper and causes murky filtrates. As a filtering agent, it is used in the preparation of numerous pharmaceutical solutions, *e. g.*, the aromatic waters, Magnesium Citrate Solution, Aromatic Elixir, N. F., Antiseptic Solution, Orange Syrup, etc.

#### NON-OFFICIAL MAGNESIUM COMPOUNDS

**Magnesium Chloride**,  $\text{MgCl}_2$ , Molecular Weight, 95.23.—Magnesium chloride is found in Nature in salt deposits, in sea water and as the mineral *carnallite* ( $\text{MgCl}_2 \cdot \text{KCl} \cdot 6\text{H}_2\text{O}$ ). It crystallizes from water as the hexahydrate ( $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ ; molecular weight, 203.34), in which form it was recognized by the Fifth Edition of the *National Formulary* as *Magnesii Chloridum*.

Magnesium chloride occurs in colorless, transparent monoclinic crystals, or as white translucent pieces. It is highly deliquescent and resembles calcium chloride in its chemical behavior by not being dehydrated by heat without being partially hydrolyzed (1).



Because of the hydrochloric acid produced upon the hydrolysis of magnesium chloride, water that contains any appreciable amount of this salt should not be used in steam boilers.

One Gm. of the salt dissolves in about 0.6 cc. of water. It is soluble in alcohol. Magnesium chloride decomposes at red heat.

1. An aqueous solution of magnesium chloride is neutral to litmus paper.

2. An aqueous solution of the salt responds to all tests for magnesium ion (*q. v.*) and for chloride ion (*q. v.*).

Magnesium chloride may be obtained by the action of hydrochloric acid upon magnesite (native magnesium carbonate). Nearly all magnesium chloride is obtained as a by-product in the preparation of potassium chloride from carnallite. The mother liquors are evaporated in open iron pans to a density of 1.4077, when the less soluble salts precipitate and are raked out. When the concentrated solution is allowed to cool, a radiating crystalline mass of  $MgCl_2 \cdot 6H_2O$  quickly forms.

Anhydrous magnesium chloride may be obtained by heating the hexahydrate in a current of hydrogen chloride or by carefully volatilizing ammonium chloride and water from the double salt,  $MgCl_2 \cdot NH_4Cl \cdot 6H_2O$ .

Magnesium chloride is used industrially for many purposes, *e. g.*, dressing cotton and woolen fabrics, fire-proofing wood, making magnesium salts, etc. Magnesia cement (sorel cement, lignolite, xylotite, etc.) is made by adding about 700 parts of a 32 per cent solution of magnesium chloride to a mixture composed of 100 parts of freshly heated magnesium oxide and 300 parts of infusorial earth or sawdust and stirring constantly until there is formed a jelly-like mass which sets to a hard solid consisting of a hydrated basic magnesium chloride of indefinite composition.

## CHAPTER XXII

### ZINC AND ZINC COMPOUNDS

#### ZINC

Symbol, Zn. Valence, II. Atomic Weight, 65.38;  
Atomic Number, 30

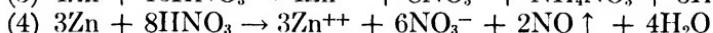
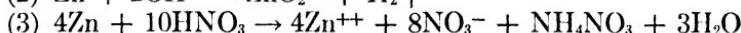
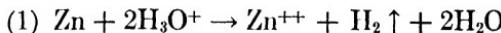
**History.**—In the writings of Aristotle, references are found to an “earth” which when fused with copper, gave a bright, light colored metal that was called the “metal of the Masynœci” (brass). Pliny also wrote about a mineral that he called *cadmia* (zinc ores). When this mineral was heated with copper, the latter was converted into *aurichalcum* (brass). He called especial attention to the fact that the deposit (zinc oxide) formed in brass furnaces could be used in place of this mineral. In 1677, Kunckel advanced the theory that “cadmia” was a “metallic calx” that dyed copper yellow by “giving its metal up to it.” The word *zinc* was first used by Paracelsus in the sixteenth century. He regarded the substance as a “semi-metal” and the word was indiscriminately used both for the metal and its ores. In 1720, Henckel prepared metallic zinc in a fair state of purity. In England, the art of zinc smelting came into being about 1730.

**Occurrence.**—Zinc does not occur free in Nature. In combination, it is widely distributed. The most important zinc ores are *sphalerite* or *zinc blende* [ZnS], the anhydrous silicate, *willemite* [Zn<sub>2</sub>SiO<sub>4</sub>], *calamine* [Zn<sub>2</sub>SiO<sub>4</sub>.H<sub>2</sub>O], and *smithsonite* [ZnCO<sub>3</sub>]. Other zinc-bearing minerals are *wurtzite* [ZnS], *zincite* [ZnO], *goslarite* [ZnSO<sub>4</sub>.7H<sub>2</sub>O], *franklinite* [(Fe, Zn, Mn)O.(Fe, Mn)<sub>2</sub>O]<sub>3</sub> and *hydrozincite* [ZnCO<sub>3</sub>.2Zn(OH)<sub>2</sub>]. Belgium, Silesia, Saxony, Poland, Spain, and England are the most noteworthy of the zinc producing European countries. In the United States, Missouri (Joplin region) produces about 50 per cent of all the zinc. Other important zinc producing states are New Jersey, Montana, Kansas, Oklahoma, Wisconsin, Idaho, and Colorado.

**Physical Properties.**—Zinc is a bluish-white, moderately hard metal that crystallizes in hexagonal prisms and pyramids. When cold, zinc is brittle. From 100° to 150° C., it becomes both malleable and ductile, but when heated at 210° to 300° C., it again becomes brittle and may be powdered in a mortar. Zinc that has been rolled into sheets remains flexible when cooled. The metal fuses at 419.4° C., and boils at 907° C. Its specific gravity is 7.14 at 20° C. The vapor density shows that it is monatomic.

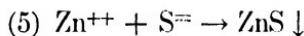
**Chemical Properties.**—Zinc is bivalent in all of its compounds. The metal is not attacked to any appreciable extent by the oxygen in the air, because it soon becomes covered with a thin coating of a

non-porous protective basic carbonate. Zinc vapor burns with a bluish-white flame, the oxide of the metal being formed. It dissolves in acids (1) and alkali hydroxides (2) (*not* ammonium hydroxide) with the evolution of hydrogen. Zinc is readily attacked by dilute nitric acid to form zinc nitrate, ammonium nitrate, and oxides of nitrogen (3). Ordinary strength nitric acid gives zinc nitrate and nitric oxide (4). The element enters into complex ions.



The zinc ion enters into several characteristic reactions as follows:

1. Ammonium sulfide  $[(\text{NH}_4)_2\text{S}]$  precipitates *white* zinc sulfide from neutral, alkaline or faintly acid solutions of a zinc salt (5). The precipitate is insoluble in acetic acid but is dissolved by diluted hydrochloric acid.

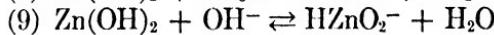


On the other hand, zinc ion is incompletely precipitated by passing hydrogen sulfide into a solution of zinc sulfate (6).

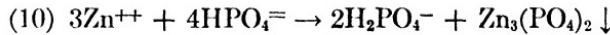


The hydronium ion from the sulfuric acid formed in the reaction reduces the concentration of the sulfide ion ( $\text{S}^{--}$ ) more and more as the reaction proceeds, and tends to reverse the reaction. Therefore, when the product of the zinc- and sulfide-ion concentrations no longer exceeds the ion-product constant for zinc sulfide, precipitation ceases. In the presence of sufficient alkali acetate to take care of the hydronium ions, precipitation is complete.

2. Fixed alkalies precipitate zinc ion as white flocculent zinc hydroxide (7), which exhibits amphoteric properties by dissolving both in acids (8) to form salts and in alkalies (9) to form zincates. It is soluble in ammonium hydroxide because of the formation of soluble tetrammino-zinc hydroxide  $[\text{Zn}(\text{NH}_3)_4(\text{OH})_2]$ .

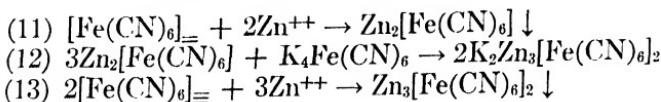


3. With a solution of a zinc salt, soluble carbonates and phosphates produce white precipitates of basic zinc carbonate or phosphate, respectively (10).



4. Alkali ferrocyanides precipitate white zinc ferrocyanides (11) which are converted into the less soluble zinc-potassium ferro-

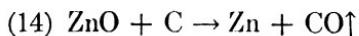
cyanides by an excess of the potassium ferrocyanide (12). Alkali ferricyanides precipitate brownish-yellow zinc ferricyanide (13).



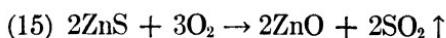
5. When a zinc salt is heated in a Bunsen flame with any cobalt salt, cobalt zincate is formed (Rimann's green). Potassium cobalticyanide is a good salt to use in this test. If test paper is to be used, it may be prepared with a solution containing 1 Gm.  $\text{K}_3\text{Co}(\text{CN})_6$ , 0.25 Gm.  $\text{KClO}_3$  in 25 cc. of  $\text{H}_2\text{O}$ .

6. When metallic zinc is placed in a solution of a tin salt that has been acidified with hydrochloric acid, the tin is precipitated in metallic form.

**Commercial Manufacture.**—It is usually necessary to concentrate zinc ores before they can be smelted profitably. This is accomplished by means of the flotation and gravity processes (p. 280). It might be mentioned that the ores mined in the Joplin districts do not average over 10 per cent of zinc. These ores are remarkable in that they are especially adapted to mechanical concentration, whereby the percentage of zinc is raised from 10 per cent to between 45 and 60 per cent. The concentrated oxide and carbonate ores are usually mixed with about one-half their weight of coal and heated in large furnaces, *e. g.*, Belgian furnace. As the temperature of the charge is raised, the carbon monoxide begins to burn with a characteristic blue flame at the mouths of the receivers and, as the temperature approaches that of reduction (about  $1200^{\circ}\text{ C.}$ ), it becomes dazzling white showing that zinc vapor is coming over (14). The first distillate collected in the specially constructed fire-clay receivers consists of about 10 per cent of zinc oxide and 90 per cent of zinc metal powder. The quantity of this material often approximates between 5 and 10 per cent of the total production and is either returned to the furnace where it assists in reducing the ore or it is sold as "zinc dust." The molten zinc that collects in the lower part of the receivers is withdrawn into large iron ladles and cast in suitable moulds into slabs, called *spelter*.



Sulfide ores cannot be reduced directly by heating with coal. Therefore, they are pulverized and roasted in suitable furnaces (15) which permit the evolved sulfur dioxide to be converted into sulfuric acid (*q. v.*). In roasting a ton of zinc ore (containing 60 per cent of zinc), a sufficient amount of sulfur dioxide is liberated to produce 1 ton of strong sulfuric acid.



Crude zinc (spelter) contains various impurities, *e. g.*, lead, iron, cadmium, antimony, arsenic, silver, copper, and sulfur. For many

years the spelter was melted in iron pans. When it was allowed to cool slowly, impurities of iron and lead collected at the bottom and zinc oxide rose to the top of the molten mass.

A very high grade zinc (99.9+ per cent) that needs no purification is now obtained by reducing high grade ores. Zinc obtained from mixed ores is always impure and large quantities are purified by electrolysis. Other electro-positive metals are precipitated from the zinc by means of zinc dust, thus reducing them to negligible amounts in the electrolyte.

**Pharmacological Action of Zinc Ion.**—The zinc ion is not used internally in therapeutics. When zinc salts are ingested there is strong local astringent action due to the precipitation of the protoplasm of the mucosa and they rarely produce any systemic effect. Excess zinc salts in the diet of animals affect reproduction and produce anemia. The parenteral administration of a soluble zinc salt produces serious symptoms such as vomiting, diarrhea, and hemorrhagic enteritis.

Zinc ion is employed in therapeutics primarily for its local actions. It exhibits astringent, corrosive and mild antiseptic properties. These effects are due to the precipitation of protein by the zinc ion.

**Uses.**—Sheet zinc is used for making roofing, gutters, etc. It is largely used for *galvanizing* iron. Sheets of iron are thoroughly cleaned with sulfuric acid or by a sand blast and immersed in a bath of molten zinc. When cold, the thin coating of zinc protects the iron from atmospheric corrosion. Other methods have been devised for applying this protective coating, *e. g.*, electroplating; covering the metal with zinc dust and baking at 800° C. (*sherardizing*); spraying molten zinc upon iron (*Shoop process*), etc. Zinc is used in batteries and in many alloys, brass (containing copper, 60 to 82 per cent and zinc 18 to 40 per cent) being the most important. Zinc metal is employed in the metallurgical processes for obtaining gold and silver (*q. v.*). Zinc dust is a fine gray powder composed of at least 90 per cent of Zn, the remainder being oxide, sulfide, etc. It is used extensively as a reducing agent in technological chemistry. Granulated zinc is made by pouring a thin stream of the molten metal into water. With acids, it is used for generating hydrogen.

#### OFFICIAL ZINC COMPOUNDS

##### ZINC ACETATE

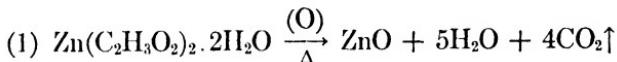
###### *Zinc Acetate*, N. F. VIII

Formula,  $\text{Zn}(\text{C}_2\text{H}_5\text{O}_2)_2 \cdot 2\text{H}_2\text{O}$ . Molecular Weight, 219.50

**Physical Properties.**—Zinc Acetate occurs as white, six-sided, monoclinic plates having a pearly luster. It has a faint odor of acetic acid and, in dilute solutions, an astringent, metallic taste. The salt has a density of 1.735 and melts at about 237° C. It gradually effloresces when exposed to the air and loses some of its acetic acid.

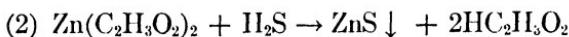
One Gm. of Zinc Acetate dissolves in 2.5 cc. of water and in 30 cc. of alcohol, at 25° C. One Gm. dissolves in 1.6 cc. of boiling water and in about 1 cc. of boiling alcohol.

When the salt is heated, it first loses water and acetic acid and, upon raising the temperature, decomposes into inflammable vapors, and a residue that is chiefly zinc oxide (1).



**Chemical Properties.**—An aqueous solution of zinc acetate is neutral or slightly acid to litmus paper. When zinc acetate is dissolved in water it exhibits all the chemical properties of the zinc ion (*q. v.*) and the acetate ion (see Sodium Acetate, p. 149).

**Official Tests for Identity.**—1. In the presence of sodium acetate, zinc ion yields a white precipitate with hydrogen sulfide (2).

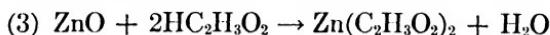


The zinc sulfide is insoluble in acetic acid but is dissolved by diluted hydrochloric acid. Ammonium sulfide produces a similar precipitate in neutral or alkaline solutions.

2. Zinc salts in solution yield with potassium ferrocyanide T.S. a white precipitate which is insoluble in diluted hydrochloric acid (*q. v.*).

3. An aqueous solution of the salt responds to all tests for *Acetate ion* (see Sodium Acetate, p. 149).

**Commercial Manufacture.**—Two parts of technical zinc oxide (or carbonate) are digested for some time with 10 parts of 18 per cent acetic acid (3). The mixture is heated to boiling, filtered while hot and the salt allowed to crystallize. A second crop of crystals may be obtained by making the mother liquor distinctly acid with acetic acid, concentrating at a temperature below its boiling-point, and allowing the salt to crystallize. Zinc acetate is purified by recrystallization from water; the product being dried without the aid of heat.



**Pharmaceutical Preparations and Uses.**—1. *Zinc Acetate* (*Zinci Acetas*), N. F. VIII.—Zinc Acetate contains not less than 82.74 per cent and not more than 87.32 per cent of  $(\text{CH}_3\text{COO})_2\text{Zn}$ , corresponding to not less than 99 per cent of the hydrated salt,  $(\text{CH}_3\text{COO})_2\text{Zn} \cdot 2\text{H}_2\text{O}$ . Zinc acetate is used locally as an astringent and mild anti-septic, particularly in cases of conjunctivitis (0.1 to 1 per cent solution) and in chronic gonorrhreal urethritis, vaginitis, etc. (0.5 to 4 per cent solution).

2. *Zinc Compounds and Eugenol Cement* (*Cämentum Zinci Compositionum et Eugenolis*, Zinc-Eugenol Cement), N. F. VIII.—This is used in dental practice along with gold, silver, etc., to fill cavities in teeth. Usually the zinc-eugenol cement is put in the cavity first and then the harder metal which provides a biting surface.

**ZINC CHLORIDE***Zinc Chloride*, N. F. VIIIFormula,  $\text{ZnCl}_2$ . Molecular Weight, 136.29

**Physical Properties.**—Zinc Chloride occurs as a white, or nearly white, odorless, crystalline powder, or in porcelain-like masses, or fused sticks or pencils. It is very deliquescent, has a specific gravity of about 2.907 at 25° C., and melts at about 290° C.

One Gm. of Zinc Chloride dissolves in 0.5 cc. of water and in about 1.5 cc. of alcohol, at 25° C. These solutions are usually slightly turbid. The turbidity disappears upon the addition of a small quantity of hydrochloric acid. It is soluble in glycerin (2 parts) and also in ether.

At about 290° C., zinc chloride fuses to a clear liquid. When heated to about 730° C., a part of the salt is volatilized as dense white fumes whereas the remainder is decomposed and leaves a residue of zinc oxide.

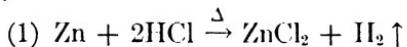
**Chemical Properties.**—An aqueous solution of zinc chloride is acid to litmus paper. The chemical properties of zinc chloride are expressed in the reactions of the zinc ion (see p. 371) and of the chloride ion (see p. 173).

**Official Tests for Identity.**—1. In the presence of sodium acetate, solutions of zinc chloride yield a white precipitate with hydrogen sulfide (*q. v.*).

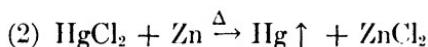
2. Ammonium sulfide and potassium ferrocyanide give characteristic reactions (*q. v.*).

**Commercial Manufacture.**—Zinc chloride may be produced by several methods.

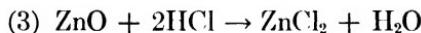
1. Zinc is heated and dry hydrogen chloride gas is passed through it (1).



2. Zinc chloride may be made by distilling a mixture of zinc and mercuric chloride (2). The mercury distills off and zinc chloride remains as a residue.



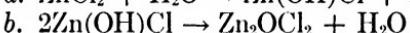
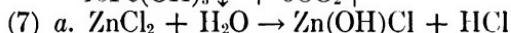
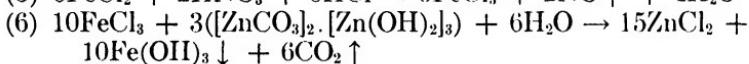
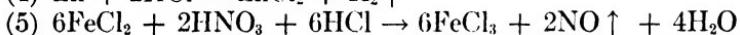
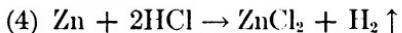
3. Hydrochloric acid will act upon zinc, zinc oxide or the carbonate to form the chloride (3).



The technical grade of zinc chloride is usually made by treating zinc with an *excess* of hydrochloric acid and evaporating to dryness. The residue is fused and poured into iron drums in which it solidifies.

The official salt may be made by dissolving the technical grade of zinc chloride in water acidulated with hydrochloric acid and evaporating the solution to crystallization. Official zinc chloride is

also prepared by a process similar to the one given in the U. S. Pharmacopoeia IX for the manufacture of the official Solution of Zinc Chloride, *viz.*, 240 Gm. of granulated zinc are digested with a mixture of 840 Gm. of hydrochloric acid and 250 cc. of distilled water until the reaction ceases (4). The liquid is decanted from the excess of zinc, mixed with 12 Gm. of nitric acid to oxidize the ferrous to ferric iron (5), and heated on a sand-bath at 115° C. to expel the excess of nitric acid and until a small portion of the liquid solidifies on cooling. The cooled, solidified mass is dissolved in about 1000 cc. of distilled water, 12 Gm. of precipitated zinc carbonate added and the mixture shaken occasionally during twenty-four hours (6). The supernatant liquid is decanted, rendered distinctly acid with hydrochloric acid to prevent hydrolysis to basic chloride (7), and concentrated until a portion solidifies upon cooling. The liquid is then poured into suitable pencil-shaped moulds and, when the salt has solidified but is still warm, it is packed in glass bottles.



**Pharmaceutical Preparations and Uses.**—*Zinc Chloride* (*Zinci Chloridum*), N. F. VIII.—Zinc Chloride contains not less than 95 per cent of  $\text{ZnCl}_2$ . It is used medicinally the same as zinc acetate and zinc sulfate. Zinc chloride is used when a more powerful escharotic action is needed such as in the treatment of malignant growths and gangrenous sores. The salt is also used in mouth washes to impart antiseptic and astringent properties to them.

### ZINC IODIDE

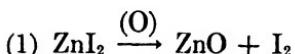
#### *Zinc Iodide*, N. F. VIII

Formula,  $\text{ZnI}_2$ . Molecular Weight, 319.22

**Physical Properties.**—Zinc Iodide is a white, or nearly white, granular powder. It is odorless, or nearly so, with a sharp, sweetish, metallic taste, and is very deliquescent. On exposure to air and light it becomes brown, due to liberation of iodine. It melts at about 446° C.

The salt is very soluble in water, freely soluble in alcohol and soluble in ether.

**Chemical Properties.**—An aqueous solution of zinc iodide is acid to litmus paper. Zinc iodide is oxidized by the oxygen in air with the liberation of iodine and the development of a brown color (1).



The presence of light and moisture speeds up the reaction.

The salt in solution gives all the reactions for the zinc ion (see p. 371) and the iodide ion (see p. 197).

**Official Tests for Identity.**—Zinc iodide responds to characteristic reactions with hydrogen sulfide, ammonium sulfide and potassium ferrocyanide (*q. v.*).

**Commercial Manufacture.**—(1) White, acicular crystals may be made by first gently heating a mixture of powdered zinc and iodine and then subliming the resulting mass or (2) granulated zinc and iodine are placed in water and digested on a water-bath. The resulting solution may then be concentrated under reduced pressure when octahedral crystals result.

**Pharmaceutical Preparations and Uses.**—1. *Zinc Iodide* (*Zinci Iodidum*), N. F. VIII.—This salt, when dried over sulfuric acid for twenty-four hours, contains not less than 98 per cent of  $\text{ZnI}_2$ . It is used as a caustic and, in solution, as an antiseptic.

2. *Iodine and Zinc Iodide Glycerite* (*Glyceritum Iodi et Zinci Iodidi*, Diluted Talbot's Solution), N. F. VIII.—The iodine is dissolved in an aqueous solution of zinc iodide (see p. 248) and then the glycerin is added. This glycerite is used in dental practice as an astringent antiseptic.

## ZINC OXIDE

### *Zinc Oxide*, U. S. P. XIII

Formula,  $\text{ZnO}$ . Molecular Weight, 81.38

**Physical Properties.**—Zinc Oxide is a very fine, odorless, white or yellowish-white, amorphous powder free from gritty particles. It has a specific gravity of about 5.47 at 20° C. When the oxide is heated to 400° or 500° C. a yellow color develops that disappears on cooling. Zinc oxide is insoluble in water and in alcohol but is soluble in dilute acids, ammonia water and ammonium carbonate T.S.

**Chemical Properties.**—Upon exposure to air it gradually absorbs carbon dioxide and is converted into a basic carbonate. It readily dissolves in dilute acids (1), in ammonia water (2) and in ammonium carbonate test solution (3).

- (1)  $\text{ZnO} + 2\text{HCl} \rightarrow \text{ZnCl}_2 + \text{H}_2\text{O}$
- (2)  $\text{ZnO} + 4\text{NH}_4\text{OII} \rightarrow \text{Zn}(\text{NH}_3)_4(\text{OH})_2 + 3\text{H}_2\text{O}$
- (3)  $\text{ZnO} + 3(\text{NH}_4)_2\text{CO}_3 \rightarrow \text{Zn}(\text{NH}_3)_4(\text{OH})_2 + 2\text{CO}_2 \uparrow + \text{H}_2\text{O}$

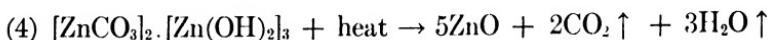
Acid solutions exhibit the reactions for the zinc ion (see, p. 371).

**Official Tests for Identity.**—1. When zinc oxide is strongly heated, it acquires a yellow color which disappears on cooling.

2. A solution of zinc oxide in dilute hydrochloric acid responds to all tests for Zinc ion (p. 374).

**Commercial Manufacture.**—*Technical Grade.*—Metallic zinc is strongly heated in earthenware retorts and the vapors, upon coming in contact with air, ignite to form the oxide, which settles out in large chambers. It is shipped in wooden kegs.

*Medicinal Grade.*—Precipitated zinc carbonate is heated to low redness (4) until a sample taken from the center of the material does not effervesce when treated with an acid. It is claimed that a whiter, softer product is obtained when the calcination is conducted over a long period of time at a low temperature (250° to 300° C.). Excessive heating results in a yellowish-white zinc oxide that is not free from gritty particles. Some manufacturers sieve their product before packaging.



**Pharmaceutical Preparations and Uses.**—1. *Zinc Oxide* (*Zinci Oxidum*), U. S. P. XIII.—Zinc Oxide, when freshly ignited, contains not less than 99 per cent of ZnO. Zinc oxide is a mild antiseptic and astringent. In the form of an ointment or dusting powder, it is employed in the treatment of eczema, impetigo, ringworm, varicose ulcers, pruritus and psoriasis. It is also used extensively in the manufacture of adhesive tape.

2. *Zinc Oxide Ointment* (*Unguentum Zinci Oxidi*, Zinc Ointment), U. S. P. XIII.—Zinc Oxide Ointment contains not less than 18.5 per cent and not more than 21.5 per cent of zinc oxide.

3. *Coal Tar Ointment* (*Unguentum Picis Carbonis*), U. S. P. XIII.—This ointment contains 25 per cent of zinc oxide.

4. *Calamine* (*Calamina*), U. S. P. XIII.—Calamine is zinc oxide with a small amount of ferric oxide, and contains, after ignition, not less than 98 per cent of ZnO. This very fine, pink, almost tasteless and odorless powder is made by calcining native zinc carbonate. In the form of powder, ointment, or lotion, it is used instead of zinc salts in various skin diseases.

5. *Calamine Lotion* (*Lotio Calaminæ*), U. S. P. XIII.—Calamine Lotion is a suspension of zinc oxide and calamine in Bentonite Magma which has been diluted with an equal volume of Calcium Hydroxide Solution. This slightly astringent, mildly alkaline preparation is used in the treatment of various skin diseases.

6. *Calamine Liniment* (*Linimentum Calaminæ*), N. F. VIII.—The liniment is a suspension of zinc oxide and calamine in an emulsion of olive oil. Calcium oleate, formed by the saponification of the olive oil with calcium hydroxide, acts as the emulsifying agent.

7. *Phenolated Calamine Lotion* (*Lotio Calaminæ Phenolata*, Compound Calamine Lotion), N. F. VIII.—It is a mixture of 99 per cent of calamine lotion and 1 per cent of liquefied phenol.

8. *Prepared Neocalamine* (*Neocalamina Præparata*), N. F. VIII.—Prepared neocalamine is zinc oxide admixed with ferric oxide, and contains, after ignition, not less than 92 per cent of ZnO. It is prepared by thoroughly mixing red ferric oxide (3 Gm.), yellow ferric oxide (4 Gm.) and zinc oxide (93 Gm.).

9. *Neocalamine Liniment* (*Linimentum Neocalaminæ*), N. F. VIII.—The prepared neocalamine is mixed with olive oil, and calcium hydroxide solution gradually added with constant agita-

tion. The calcium oleate assists in keeping the neocalamine in suspension.

10. *Neocalamine Lotion* (*Lotio Neocalaminæ*), N. F. VIII.—The neocalamine is carefully mixed with diluted Bentonite Magma. The preparation should be shaken thoroughly before dispensing.

11. *Phenolated Neocalamine Lotion* (*Lotio Neocalaminæ Phenolata*, Compound Neocalamine Lotion), N. F. VIII.—One per cent of liquefied phenol is mixed with neocalamine lotion.

12. *Neocalamine Ointment* (*Unguentum Neocalaminæ*), N. F. VIII.—This ointment contains 15 per cent of Prepared Neocalamine.

13. *Compound Resorcinol Ointment* (*Unguentum Resorcinolis Compositum*), N. F. VIII.—This contains 6 per cent of zinc oxide.

14. *Mild Resorcinol Paste* (*Pasta Resorcinolis Mitis*, Lassar's Mild Resorcinol Paste), N. F. VIII.—This paste contains, in each 100 Gm., not less than 9.5 Gm. and not more than 10.5 Gm. of  $C_6H_4(OH)_2$ , and not less than 24 Gm. and not more than 26 Gm. of ZnO.

15. *Strong Resorcinol Paste* (*Pasta Resorcinolis Fortis*, Lassar's Stronger Resorcinol Paste), N. F. VIII.—This paste contains, in each 100 Gm., not less than 19 Gm. and not more than 21 Gm. of  $C_6H_4(OH)_2$  and not less than 19 Gm. and not more than 21 Gm. of ZnO. It is used as a mild astringent and antiseptic.

16. *N. F. Sun Cream* (*Cremor Solis N. F.*, Sun Tan Ointment), N. F. VIII.—This contains 10 per cent of neocalamine.

17. *Compound Tar Ointment* (*Unguentum Picis Compositum*), N. F. VIII.—This ointment contains 3 per cent of zinc oxide.

18. *Zinc Compounds and Eugenol Cement* (*Cæmentum Zincii Compositionum et Eugenolis*, Zinc-Eugenol Cement), N. F. VIII.—Zinc oxide constitutes 70 per cent of the powder (see p. 374).

19. *Zinc Oxide Paste* (*Pasta Zincii Oxidi*, Lassar's Plain Zinc Paste), N. F. VIII.—This paste contains 25 per cent zinc oxide.

20. *Zinc Oxide Hard Paste* (*Pasta Zincii Oxidi Dura*, Unna's Hard Zinc Paste), N. F. VIII.—A smooth paste is obtained by thoroughly triturating a mixture of zinc oxide (25 Gm.) and purified siliceous earth (5 Gm.) with benzoinated lard (70 Gm.).

21. *Zinc Oxide Soft Paste* (*Pasta Zincii Oxidi Mollis*, Unna's Soft Zinc Paste), N. F. VIII.—A mixture of very finely powdered zinc oxide and precipitated calcium carbonate is triturated to a smooth paste with a soap (calcium oleate) that has been made previously by adding a solution of calcium hydroxide to linseed oil that has been heated to between 60° and 65°.

22. *Zinc Oxide Paste with Salicylic Acid* (*Pasta Zincii Oxidi cum Acido Salicylico*, Lassar's Zinc Paste with Salicylic Acid), N. F. VIII.—This paste contains 2 per cent of salicylic acid incorporated in Zinc Oxide Paste.

23. *Glycerogelatins* (*Glycerogelatina*), N. F. VIII.—The Glycerogelatins are soft masses, melting at body temperature, composed of gelatin, glycerin, water, and a medicament suitable for application in dermatological practice. The National Formulary makes it optional

whether the medicaments, *e. g.*, salicylic acid, iodoform, resorcinol, chrysarobin, etc., be used by themselves or with the addition of zinc oxide.

**Other Uses.**—The technical grade of zinc oxide (zinc white, Chinese white) is used as a pigment in paints. It has the advantage over white lead by not being darkened by hydrogen sulfide. It is also used as a filler in rubber goods, *e. g.*, automobile tires, erasers, etc. It is the source of nearly all zinc salts.

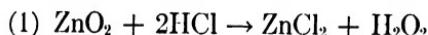
### ZINC PEROXIDE

#### *Medicinal Zinc Peroxide*, U. S. P. XIII

Formula,  $\text{ZnO}_2$

**Physical Properties.**—*Medicinal Zinc Peroxide* is a white, or faintly-yellow, fine, odorless powder. It is almost insoluble in water and in organic solvents. Dilute acids dissolve it with decomposition. The dry powder may be heated to  $140^\circ \text{ C}$ . without decomposition but it is unstable at higher temperatures.

**Chemical Properties.**—Diluted mineral acids react to form hydrogen peroxide and a soluble zinc salt (1).



Although it appears to be insoluble in water there is a slow decomposition with the liberation of hydrogen peroxide.

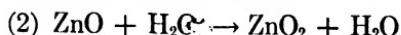
After boiling to remove the hydrogen peroxide, an acid solution will give the reactions for the zinc ion (see p. 370).

A fresh acid solution of the peroxide is a good oxidizing agent and will give those reactions characteristic of hydrogen peroxide (see *Hydrogen Peroxide*, p. 56).

**Official Tests for Identity.**—1. A solution of *Medicinal Zinc Peroxide* in a slight excess of diluted hydrochloric acid, and boiled to remove the hydrogen peroxide formed, (1) responds to the tests for zinc (see p. 370).

2. When a small quantity of the peroxide is shaken with a few cc. of water and 1 drop of diluted sulfuric acid, and a few cc. of ether and a few drops of potassium dichromate T.S. added, the water layer becomes blue; on shaking the mixture the blue color passes into the ether. This blue ether solution contains a higher oxygen compound of chromium (see p. 56). On standing over dilute acid, the solution in ether slowly loses its color and the dilute acid becomes green, due to the formation of a chromic salt.

**Commercial Manufacture.**—*Medicinal Zinc Peroxide* is a special grade both in purity and particle size. It was developed by the research laboratories of DuPont in collaboration with Dr. Frank L. Meleney from 1934 to 1938. It is prepared from very pure zinc oxide and hydrogen peroxide (2).



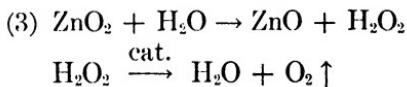
**Pharmaceutical Preparations and Uses.**—1. *Medicinal Zinc Peroxide* (*Zinci Peroxidum Medicinale*), U. S. P. XIII.—Medicinal Zinc Peroxide consists of a mixture of zinc peroxide, zinc carbonate and zinc hydroxide. It contains not less than 45 per cent of  $ZnO_2$ . The material is supplied as a dry powder and should be sterilized before using. It can be kept for about a month following sterilization, but deteriorates at that time because the heat used in sterilization also activates the evolution of oxygen.

The compound is of value in controlling surgical infections resulting from micro-aërophilic and anaërobic bacteria. In general, one can state that the more strict an organism is in its oxygen requirements, the more susceptible it is to the action of zinc peroxide. Many types of wounds are suspected of harboring anaërobic bacteria. Gunshot wounds, human bites, most puncture and deep surgical wounds are among them.

Zinc peroxide is used by mixing it with water to form a heavy creamy suspension which is distributed over the surface of the wound, wrapped with gauze and then coated with petrolatum or zinc ointment to make the dressing air-tight.

Formulas for making ointments and suspensions have been published.<sup>1</sup>

No doubt the activity of zinc peroxide is due to the release of oxygen by the following mechanism (3).



### ZINC STEARATE

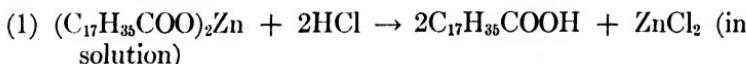
#### *Zinc Stearate*, U. S. P. XIII

**Physical Properties.**—Zinc Stearate is a fine, white, bulky powder, free from grittiness, having a faint, characteristic odor. It is unctuous to the touch and readily adheres to the skin.

It is insoluble in water, in alcohol, and in ether.

**Chemical Properties.**—The salt fuses when heated to about 120° C. It decomposes at higher temperatures into inflammable vapors having the odor of burning fat, and zinc oxide containing some free carbon. When the compound is placed on moist litmus paper no change of color is observed.

When Zinc Stearate is heated with about 5 per cent hydrochloric acid, stearic acid is liberated and floats as an oily layer on the surface of the liquid (1).



The aqueous solution obtained in (1) should respond to all tests for zinc ion (see p. 370).

The stearic acid may be separated and tested.

<sup>1</sup> J. Am. Pharm. Assn., Pr. Ed., 3, 7 (1942).

**Official Tests for Identity.**—1. Zinc stearate is hydrolyzed with hydrochloric acid to stearic acid and a solution of zinc chloride (1). This acid solution responds to all the tests for Zinc (see p. 370).

2. Stearic acid may be isolated by treatment with water, sulfuric acid and heat. The solidification temperature of the fatty acid is not below 54° C. (see U. S. P. XIII, p. 612).

**Commercial Manufacture.**—Zinc stearate is usually made by decomposing a boiling solution of sodium stearate (animal or curd soap) with a hot solution of either zinc acetate or sulfate (2). The precipitate is washed with hot water, dried, powdered, and sieved. A much superior product may be obtained by decomposing a sodium stearate that has been prepared by adding stearic acid to a hot solution of sodium carbonate (3).



**Pharmaceutical Preparations and Uses.**—1. *Zinc Stearate* (Zinci Stearas), U. S. P. XIII.—Zinc Stearate is a compound of zinc with variable proportions of stearic acid and palmitic acid containing the equivalent of not less than 13 per cent and not more than 15.5 per cent of ZnO.

Zinc stearate is mildly antiseptic and astringent. It is used as a dusting powder for treating inflammatory skin diseases. It is also employed in the form of an ointment.

2. *Zinc Compounds and Eugenol Cement* (Caementum Zinci Compositionum et Eugenolis, Zinc-Eugenol Cement), N. F. VIII.—One Gm. of Zinc Stearate is used in making up the powder (see p. 374).

### ZINC SULFATE

#### *Zinc Sulfate*, U. S. P. XIII

Formula,  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ . Molecular Weight, 287.55

**Physical Properties.**—Zinc Sulfate occurs in the form of colorless transparent, rhombic prisms or needles, or as a granular, crystalline powder, odorless, and having an astringent, metallic taste. It effloresces in dry air. It has a specific gravity of about 1.967 at 16.5° C.

One Gm. of Zinc Sulfate dissolves in 0.6 cc. of water and in about 2.5 cc. of glycerin, at 25° C. It is insoluble in alcohol.

The salt melts at about 50° C. When strongly ignited, it decomposes, losing both water and sulfuric acid.

**Chemical Properties.**—Zinc sulfate (like cupric sulfate) combines with potassium and ammonium sulfates to form double salts, *e. g.*,  $\text{ZnSO}_4 \cdot \text{K}_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ . These compounds exist as such only in the solid state. When they are dissolved in water, they separate into the respective components, which in turn dissociate into their respective ions. The salt produces a solution that is acid to litmus paper

and exhibits all the reactions of the zinc ion (see p. 370) and the sulfate ion (see p. 131).

**Official Test for Identity.**—Its aqueous solutions respond to all tests for Zinc ion (see p. 370) and for Sulfate ion (see p. 134).

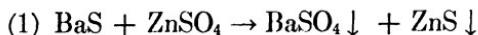
**Commercial Manufacture.**—1. Commercial zinc sulfate is made by roasting zinc sulfide ore (blende) in the presence of air under very specific conditions of temperature and amount of air used. The zinc sulfate formed by the oxidation of the sulfide is dissolved in hot water and the solution concentrated to crystallization.

2. The U. S. Pharmacopoeia grade of zinc sulfate is usually made by digesting an excess of granulated zinc in diluted sulfuric acid. The resulting solution is filtered and treated with chlorine water, which oxidizes any ferrous sulfate to ferric sulfate. The ferric ion is precipitated as hydroxide by agitating the solution with either zinc oxide or precipitated zinc carbonate. The mixture is filtered, the filtrate concentrated, and the salt allowed to crystallize. The product should be free from heavy metals (arsenic, copper, lead, iron, etc.), alkali metals, alkaline earth metals, and free acid.

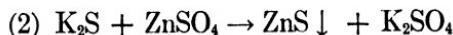
**Pharmaceutical Preparations and Uses.**—1. *Zinc Sulfate* (Zinci Sulfas), U. S. P. XIII.—Zinc Sulfate contains not less than 55.6 per cent and not more than 61 per cent of  $ZnSO_4$ , corresponding to not less than 99 per cent of the hydrated salt ( $ZnSO_4 \cdot 7H_2O$ ).

Zinc sulfate is used as an emetic and astringent. It acts so quickly upon the vomiting reflex that emesis is produced before there is time for any other local irritant effect. It is an excellent emetic to use for emptying the stomach of undigested foods and non-corrosive poisons. It is employed also in 0.1 to 1 per cent solution as collyria.

The technical grade of zinc sulfate is used as a mordant in dyeing and as a preservative for woods and skins. When zinc sulfate and barium sulfide are allowed to react in a special way, a mixture of barium sulfate and zinc sulfide results (1). When this material is washed, ignited, suddenly cooled, ground, washed and dried, it is known as *lithopone*. When this is made into a paint, it has greater spreading power than white lead and also has the advantage of not being darkened by hydrogen sulfide. Lithopone paints are dulled by direct sunlight.



2. *White Lotion* (Lotio Alba, Lotio Sulfurata), N. F. VIII.—A filtered solution of sulfurated potash is added slowly and with constant stirring to a filtered solution of zinc sulfate (2).



In the alkaline solution, the precipitation of the zinc as sulfide is practically complete, potassium sulfate remaining in solution. This preparation should be freshly prepared and shaken thoroughly before dispensing.

It is used in skin diseases for the sulfide effect. The zinc ion provides an astringent action.

3. *Compound Zinc Sulfate Powder* (*Pulvis Zinci Sulfatis Compositus*), N. F. VIII.—Boric acid is the main ingredient. It contains 12.5 per cent of zinc sulfate. The preparation is soluble in water and is used as an antiseptic and astringent.

#### NON-OFFICIAL ZINC COMPOUNDS

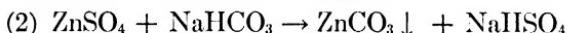
**Zinc Carbonate**,  $\text{ZnCO}_3$ , Molecular Weight, 125.39.—Normal zinc carbonate is found as *smithsonite* and *hydrozincite* in rhombohedral crystals that are isomorphous with *calcite*. Its formation in Nature is attributed to zinc sulfate-bearing waters attacking limestone (1).



Impure native zinc carbonate is often contaminated with small quantities of iron that give the powdered material a light brown color. This is known in commerce as *calamine*, *Lapis Calaminaris*, *Zinkspath*, etc. This product should not be confused with the official *Calamine* which is principally zinc oxide.

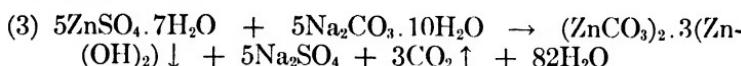
Normal zinc carbonate is marketed only in a technical grade. It is a white, odorless and tasteless, crystalline powder, having a density of about 4.43. It is insoluble in water and alcohol, but dissolves in acids, in alkalies, and in solutions of ammonium salts. When heated to about 300° C., it loses carbon dioxide and leaves a residue of zinc oxide.

It is obtained by grinding the mineral smithsonite or by the action of sodium bicarbonate upon solutions of zinc salts (2). The product contains zinc oxide and hydroxide as impurities. It can be, but seldom is, purified by crystallization. It is packed in wooden barrels or tins and is used as a pigment.



**Precipitated Zinc Carbonate.**—Precipitated zinc carbonate is a basic carbonate having a somewhat variable chemical composition. It is a white, odorless and tasteless, impalpable powder which is insoluble in water and in alcohol but dissolves in dilute acids, in ammonia water, and in solutions of ammonium carbonate.

The salt is prepared by dissolving 10 parts of crystallized zinc sulfate ( $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ ) in 50 parts of water and slowly adding the solution to a boiling, filtered solution of 11 parts of sodium carbonate ( $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$ ) in 60 parts of water. The solution is stirred constantly during the addition. After boiling for about fifteen minutes, the precipitate becomes granular and readily subsides. The precipitate is washed with hot water until it is free from sulfates and dried at about 50° C. The reaction may be represented by the following equation (3).



Basic zinc carbonate was recognized by the U. S. Pharmacopœia IX under the title *Zinci Carbonas Præcipitatus*, and was required to contain basic zinc carbonate corresponding to not less than 68 per cent of zinc oxide.

Basic zinc carbonate is used for its protective and mild antiseptic and astringent properties. It is applied in the form of an ointment or dusting powder.

**Zinc Permanganate.**—This salt consists of dark brown crystals which are freely soluble in water. It releases oxygen just as potassium permanganate but it *must be handled with greater care*. The chemical properties in solution are characteristic of the permanganate ion (see Pot. salt, p. 252) and the zinc ion (see p. 370). Like potassium permanganate, it is used in medicine as an oxidizing antiseptic.

## CHAPTER XXIII

### CADMIUM AND CADMIUM COMPOUNDS

#### CADMIUM

Symbol, Cd. Valence, II. Atomic Weight, 112.41; Atomic Number, 48

**History and Occurrence.**—This metallic element was discovered in 1817 by F. Stromeyer. He showed that the yellow color of a particular sample of iron-free zinc oxide was due to the presence of the oxide of a new metal. He named the element *cadmia fornacum* ("furnace zinc") because he found the substance also in the zinc dust or first runnings obtained in the distillation of zinc. At about the same time, Hermann, a manufacturing chemist of Schönebeck, showed that a specimen of zinc oxide that was thought to contain arsenic, really contained the oxide of a new element.

Cadmium does not occur as such in Nature. In combination as the carbonate or sulfide, it occurs in small amounts (about 0.5 per cent) in the corresponding zinc ores (zinc blende, calamine, etc.). The rare mineral *greenockite*, found in Scotland, Bohemia, Pennsylvania and Missouri, consists largely of cadmium sulfide.

**Physical Properties.**—Cadmium is a white metal, having a slight bluish tinge. It is quite stable in dry air, but in moist air it becomes covered with a film of the oxide. It readily takes a high polish. It is a little harder than tin, but is softer than zinc. The metal is ductile and malleable. It has a specific gravity of 8.65 (20°); melts at about 320.9° C.; and boils at 767° C., forming a deep yellow vapor. It is insoluble in water. The vapor density shows it to be monatomic.

**Chemical Properties.**—Cadmium is always bivalent and enters into complex ions, *e. g.*,  $\text{Cd}(\text{NH}_3)_4^{++}$ . Its oxide and hydroxide are basic, and its salts are not hydrolyzed. Like the halides of zinc and mercury, these salts of cadmium are only slightly ionized in concentrated solution. This is due to the fact that they form autocomplexes and also because their crystal structure shows them not to be true ionic compounds. It immediately precedes iron in the electromotive series and hence displaces hydrogen from dilute acids. Cadmium unites with a number of the heavy metals to form alloys. The melting-point of an alloy is usually lowered by cadmium and hence it finds a useful application in the so-called *fusible alloys*. The amalgams which it forms with mercury are employed as fillings in dentistry.

Some of the characteristic reactions of the cadmium ion are as follows: 1. Hydrogen sulfide precipitates a bright yellow cadmium sulfide from neutral or alkaline solutions of cadmium salts (1). Cad-

mium sulfide is insoluble in alkali hydroxides, in alkali sulfides, *e. g.*, NaHS (distinction from arsenic) and in cold diluted acids. It is soluble in cold, moderately diluted nitric acid, in hot diluted hydrochloric acid, or in hot, moderately diluted sulfuric acid. The formation of a yellow sulfide in alkaline solution is a distinctive test for cadmium ion as arsenic and tin sulfides are relatively soluble under the conditions.

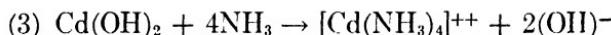


In moderately strong acid solutions (2 to 9 per cent H<sub>2</sub>SO<sub>4</sub> or 0.5 to 1.8 per cent HCl) a yellow changing quickly to orange colored precipitate is thrown down. The precipitate is not pure CdS but contains more or less Cd<sub>2</sub>(SO<sub>4</sub>)S or Cd<sub>2</sub>Cl<sub>2</sub>S.

2. Alkali hydroxides precipitate a white cadmium hydroxide [Cd(OH)<sub>2</sub>] from solutions of cadmium salts (2). It is insoluble in excess of reagent.



3. Ammonium hydroxide forms the same precipitate [Cd(OH)<sub>2</sub>] as in (2). The cadmium hydroxide dissolves in an excess of the precipitant (difference from lead) (3).



**Commercial Manufacture.**—Cadmium is usually obtained from the first flue-dust caught in the sheet iron adapters of zinc retorts. On account of the relatively low boiling-point of cadmium (767° C.) as compared to zinc (907° C.), cadmium distils over first. This "zinc dust" is mixed with coal and distilled at the lowest possible temperature, thus obtaining a distillate that is rich in cadmium and cadmium oxide. The crude product is dissolved in sulfuric acid and the cadmium precipitated with hydrogen sulfide (zinc is not precipitated by H<sub>2</sub>S in acid solution). The cadmium sulfide is then dissolved in concentrated hydrochloric acid, precipitated as the carbonate (CdCO<sub>3</sub>-white, insoluble in excess) with ammonium carbonate (Cu and As remaining in solution) and the product calcined. The cadmium oxide is mixed with charcoal and distilled and the metallic distillate is collected in suitable receivers. The metal is purified by dissolving it in hydrochloric acid and digesting the solution with metallic zinc, which replaces cadmium from solutions of its salts.

**Pharmacological Action of Cadmium Ion.**—Cadmium ion closely resembles zinc ion in its action, but is more toxic. The chloride is a powerful emetic. Systemically it is said to behave like mercury and after absorption, produces death by arresting respiration. In cases of poisoning it is found chiefly in the liver and kidney.

**Uses of Cadmium.**—Cadmium is used to electroplate those metals in which no high polish or luster is desired. It apparently forms an alloy with the surface metal, does not peel or flake off, and

hence is superior to the other metals for rust-proofing. It is a constituent of easily fusible alloys, *e.g.*, Wood's Metal, Rose's Metal, etc.

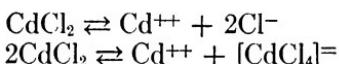
#### NON-OFFICIAL CADMIUM COMPOUNDS

**Cadmium Oxide** ( $\text{CdO}$ ).—Cadmium oxide is a yellowish-red to brownish-black, amorphous powder having a specific gravity of 8.15 at  $20^\circ\text{ C}$ . It is prepared by heating the metal in air or oxygen, or by calcining the carbonate or nitrate. It possesses basic properties and readily dissolves in acids to form colorless solutions from which the salts may be obtained.

**Cadmium Hydroxide** [ $\text{Cd}(\text{OH})_2$ ].—Cadmium hydroxide is a white powder obtained by adding a fixed alkali hydroxide to a solution of a cadmium salt and drying the precipitate. It is insoluble in an excess of the precipitant, but dissolves in ammonium hydroxide to form a complex hydroxide,  $\text{Cd}(\text{NH}_3)_4(\text{OH})_2$ . The powder has a specific gravity of 4.79 at  $15^\circ\text{ C}$ ., and decomposes when heated to  $300^\circ\text{ C}$ . It is an excellent absorbent for carbon dioxide.

**Cadmium Carbonate** ( $\text{CdCO}_3$ ).—A white, water-insoluble powder obtained when a solution of an alkaline carbonate is added to a solution of a cadmium salt.

**Cadmium Chloride** ( $\text{CdCl}_2 \cdot 2\frac{1}{2}\text{H}_2\text{O}$ ), **Cadmium Bromide** ( $\text{CdBr}_2 \cdot 4\text{H}_2\text{O}$ ), **Cadmium Iodide** ( $\text{CdI}_2$ ).—The cadmium salts of the hydrohalogen acids are colorless, stable compounds that are readily soluble in alcohol and in water. The chloride is usually made by dissolving the oxide in hydrochloric acid. It is thought by some that the chloride and also the bromide and iodide when dissolved in water behave as follows:



Cadmium chloride occurs as small, colorless crystals that effloresce in dry air. The bromide and iodide are prepared by digesting the metal with either bromine or iodine in the presence of water. These compounds form double salts with the salts of the alkalies. Cadmium potassium iodide,  $\text{CdI}_2 \cdot 2\text{KI} \cdot 2\text{H}_2\text{O}$ , is a useful reagent in testing for alkaloids and for peroxides in ether. On account of its solubility in alcohol, cadmium iodide is used to some extent in photography.

**Cadmium Nitrate** [ $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ ].—Cadmium nitrate is made by dissolving the metal in nitric acid. It occurs as fibrous, very deliquescent needles which are very soluble both in alcohol and in water. It is used as a reagent (Browning-Palmer test for ferri-cyanides) and to give a reddish-yellow luster to glass.

**Cadmium Sulfate** [ $(\text{CdSO}_4)_3 \cdot 8\text{H}_2\text{O}$ ].—Cadmium sulfate occurs in the form of large crystals, which are deposited when a concentrated aqueous solution of the salt is allowed to evaporate spontaneously. The salt is used as an astringent in ophthalmic practice. It has been used for making standard electric cells such as the Weston cell.

**Cadmium Sulfide** (CdS).—Cadmium sulfide occurs in Nature as the mineral *greenockite*. It is deposited as a bright yellow precipitate when hydrogen sulfide is passed into a solution of a cadmium salt. Because it is not affected by hydrogen sulfide, it is employed alone as a yellow pigment ("cadmium yellow," "Jaune Brilliant," etc.) or in admixture with ultramarine as a green pigment. It is also used as a yellow or orange color for soaps, ink, glass, paper, textiles, rubber, fireworks, etc.

## CHAPTER XXIV

### MERCURY AND MERCURY COMPOUNDS

#### **MERCURY**

##### *Mercury, U. S. P. XIII*

Symbol, Hg. Valence, I, II. Atomic Weight, 200.61;  
Atomic Number, 80

**History.**—Apparently this element was unknown to the ancient Jews and no mention was made of it by the early Greek writers. Theophrastus (about 300 b.c.) described it as *liquid silver* or *quick-silver*, and stated that it could be obtained from *cinnabar* (HgS) by treatment with copper and vinegar. In the first century, Dioscorides obtained it from the same mineral by sublimation with charcoal. Pliny named the liquid metal *hydrargyrum* from the Graeco-Latin *ὕδωρ*, water, and *ἀργυρός*, silver. The metal has always been associated with the planet Mercury, from which it takes its present name. Geber held that the predominant element in this liquid substance entered into the composition of all metals, and in fact was the cause of metallicity. His theory was accepted quite generally and led to many attempts to convert the baser metals into silver and gold.

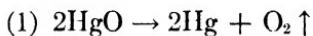
**Occurrence.**—Mercury occurs in Nature chiefly as the red crystalline sulfide called *cinnabar*. It is found also in small globules disseminated through rocks, and as an amalgam of silver and gold. The principal deposits of cinnabar are found in Spain (Almaden), Illyria (Idria), United States (California, Nevada and Texas), Japan, China and Mexico. Mexico has been producing a sizeable quantity per month.

**Physical Properties.**—At ordinary temperatures, mercury is a bright, shining, silvery-white metal, liquid at ordinary temperatures, and easily divisible into spherical globules. At  $-38.89^{\circ}$  C., it forms a white malleable and ductile solid, which exhibits cubical crystals. It boils at  $356.9^{\circ}$  C. It has a specific gravity of 13.546 at  $20^{\circ}$  C. and has a noticeable vapor tension at ordinary temperatures (0.0002 mm. at  $0^{\circ}$  C. to 0.0013 mm. at  $20^{\circ}$  C.). Mercury expands rapidly and uniformly when heated and because of its wide range of fluidity, it is used in making thermometers. Mercury vapor is colorless and its density indicates that the molecules are monatomic. Superheated mercury vapor is a conductor of electricity and, when acting as such, radiates light that is rich in ultra-violet rays. The mercury lamp, used in the sterilization of water, consists of a quartz tube about 50 or 60 cm. long in which there is a very high vacuum. The two poles are united by a thin thread of mercury. When the current is turned on, the mercury is rapidly heated and

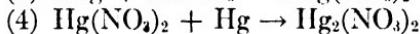
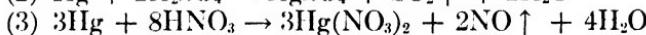
the vapors readily conduct the current and become incandescent by doing so. As soon as a sufficient amount of the mercury has been vaporized to carry the current, the tube should be inclined in order to collect all of the mercury at one end. Mercury amalgamates with most of the familiar metals, excepting iron and platinum.

**Chemical Properties.**—The consideration of the chemistry of mercury is best taken up under the following headings: (1) metallic mercury; (2) mercurous compounds, and (3) mercuric compounds.

1. At ordinary temperatures, *mercury* is permanent in air, ammonia, carbon dioxide, nitrous oxide and in some other gases. When heated near its boiling-point in air, the metal slowly combines with oxygen to form red mercuric oxide ( $HgO$ ), which decomposes at higher temperatures into the free metal and oxygen (1). Sulfur and the halogens combine directly with it. This may be demonstrated by triturating mercury and iodine together to form mercuric iodide.



The position of mercury in the electromotive series makes it insoluble in many of the common acids. However, it is soluble in the oxidizing acids, such as hot concentrated sulfuric acid (2) and cold nitric acid (3). In the latter case, the NO which is evolved is readily oxidized by atmospheric oxygen to nitrogen dioxide (brown). If to the mercuric nitrate which is obtained in reaction (3) is added an excess of metallic mercury, the mercurous salt is formed (4).



It is interesting to note that although mercury is below hydrogen in the electromotive series it is acted upon by one of the hydrohalide acids, namely, hydriodic acid. Hydriodic acid dissolves mercury readily with the evolution of hydrogen (5), although hydrochloric and hydrobromic acids are without appreciable effect. The reason for its solution in hydriodic acid follows from the fact

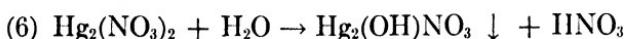


that even metals below hydrogen in the electromotive series and in sufficiently dilute solution can be oxidized by hydronium ion (hydrogen ion). This fact, together with the knowledge that the  $HgI_4^-$  ionizes only slightly into  $Hg^{++}$  and  $I^-$  (ionization constant of  $HgI_4^- = 5 \times 10^{-31}$ ), shows why the hydronium ion can act in this case as an oxidizing agent and in that manner dissolve mercury. Mercury resembles copper by forming two series of compounds, *viz.*, mercurous (bivalent  $Hg_2^+$ )<sup>1</sup> and mercuric (bivalent

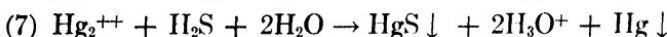
<sup>1</sup> The bivalent mercurous ion,  $Hg_2^{++}$ , is used here since it has been shown more or less conclusively that mercurous mercury exists in this form both in solutions and in compounds. The older method of writing mercurous ion (still retained by the U. S. P. XIII) is  $Hg^+$ .

Hg). Also, the mercurous halides, like the cuprous halides, are nearly insoluble in water and are decomposed by light. Both mercurous and mercuric hydroxides lose water spontaneously and are changed into the corresponding oxides ( $\text{Hg}_2\text{O}$  and  $\text{HgO}$ ). These oxides are very feebly basic and hence their salts are easily hydrolyzed to basic salts. Mercury enters into a number of complex ions, *e. g.*,  $\text{HgCl}_4^-$ ,  $\text{HgBr}_4^-$ ,  $\text{Hg}(\text{CN})_4^-$ , etc.

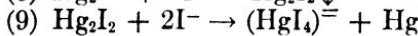
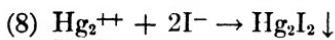
2. *Mercurous salts*, in general, are prone to split off an atom of mercury to form the more stable mercuric series. Soluble mercurous salts, *e. g.*, the nitrate (6), tend to hydrolyze in aqueous solution to form basic salts.



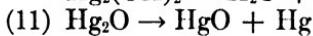
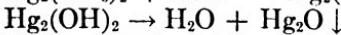
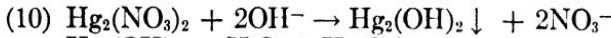
Hydrogen sulfide or soluble sulfides precipitate black mercuric sulfide and mercury (gray) from solutions of mercurous salts (7). Mercurous sulfide ( $\text{Hg}_2\text{S}$ ) does not exist at ordinary temperatures.



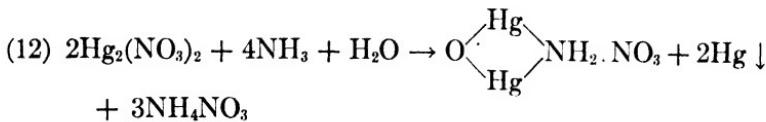
Soluble iodides precipitate mercurous ion as the yellow mercurous iodide (8) which is insoluble in water and in alcohol. The precipitate may become green upon standing. The precipitate is partly soluble in an excess of precipitant (9).



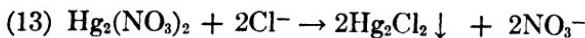
Fixed alkali hydroxides precipitate mercurous ion as black-brown mercurous oxide (10) which is insoluble in alkali but is readily transposed by acids. It is very unstable toward heat and light (11).



From solutions of mercurous salts, ammonium hydroxide precipitates *mixtures* of mercury and mercuric ammonium compounds (12).

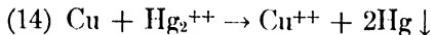


Hydrochloric acid and soluble chlorides precipitate white mercurous chloride from solutions of mercurous salts (13). The precipitate is insoluble in water but slowly soluble in hot concentrated hydrochloric acid. It is blackened by ammonia T.S. (*i.e.* 12)

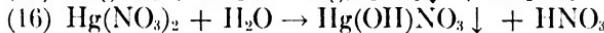
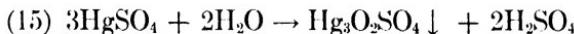


When a piece of bright copper is immersed in a solution of a mercury salt that is free from excess of nitric acid, it becomes coated with a dark film of metallic mercury (14), which may be

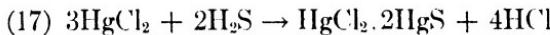
given a bright and silvery polish by rubbing. The deposit is readily volatilized by heat. Copper, like all of the elements above mercury in the electromotive series, has a greater tendency toward the ionic than mercury and hence will displace the latter from solutions of its salts.



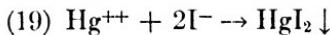
3. *Mercuric salts* are similar to mercurous in that they are also readily hydrolyzed to form insoluble basic salts. This is especially true of the sulfate (15) and nitrate (16). The presence of an excess of acid prevents the formation of these basic salts.



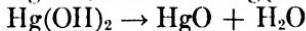
Hydrogen sulfide or soluble sulfides precipitate black mercuric sulfide from solutions of mercuric salts (17). The precipitate is first white ( $\text{HgCl}_2 \cdot 2\text{HgS}$ , a union of the original mercuric salt with mercuric sulfide) (18), then yellow (unions having greater proportions of  $\text{HgS}$ ), then brown, and finally black.



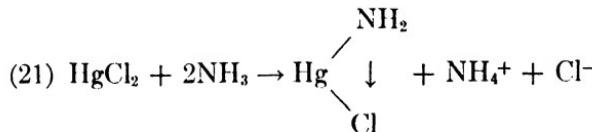
Soluble iodides precipitate mercuric ion as scarlet, microcrystalline mercuric iodide (19). The precipitate is yellow at first but quickly changes to a scarlet color. It is very insoluble in water, but readily dissolves in ether, in alcohol, and in an excess of potassium iodide. With the latter, it forms the complex compound potassium mercuri-iodide ( $\text{K}_2\text{HgI}_4$ ) which dissociates into potassium ion and the complex anion,  $\text{HgI}_4^-$ . A solution of this salt is known as Mayer's Reagent.



Fixed alkali hydroxides precipitate yellow mercuric oxide from solutions of mercuric salts (20). The hydroxide that is first formed, spontaneously decomposes into the oxide and water.

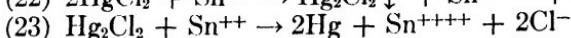


Ammonium hydroxide precipitates white mercuric amido chloride from a solution of mercuric chloride (21).

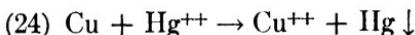


Stannous chloride precipitates white, insoluble mercurous chloride (22) from solutions of mercuric salts. By heating the precipi-

tate in an excess of the precipitant, it turns gray, due to the reduction of the mercurous chloride to metallic mercury (23).



Mercuric salts, like mercurous salts, deposit mercury on the surface of copper foil (24).



**Official Tests for Identity.**--1. Solutions of mercury salts which are free from an excess of nitric acid will deposit mercury upon a bright copper foil (14, 24), the deposit becoming bright and silvery upon rubbing.

2. Solutions of mercury compounds yield a black precipitate (7, 17, 18) which is insoluble in ammonium sulfide T.S., or in boiling diluted nitric acid.

*Mercuric Salts.*—(a) Mercuric salts yield a yellow precipitate of yellow mercuric oxide when treated with sodium hydroxide T.S. (20).

(b) In neutral solutions, mercuric salts yield a scarlet precipitate of mercuric iodide with potassium iodide T.S. (19). This precipitate is soluble in an excess of the reagent (25).



*Mercurous Salts.*—(a) Sodium hydroxide T.S. decomposes mercurous compounds forming a black color due to mercurous oxide (10).

(b) Hydrochloric acid added to solutions of mercurous salts produces a white precipitate which is blackened by ammonia T.S. (13).

(c) Potassium iodide T.S. produces a yellow precipitate of mercurous iodide (8) which may turn green on standing.

**Commercial Manufacture.**—Mercury is readily obtained by roasting its principal ore (cinnabar,  $\text{HgS}$ ) in huge shaft furnaces (capacity about 50 tons of ore) at a temperature above  $360^\circ \text{ C}$ . with access of air. Any mercuric oxide formed during the roasting is instantly decomposed into mercury and oxygen at the temperature of the process. The vapors are condensed in a series of stone towers in which the ascending gases are cooled by a descending spray of water and the mercury is collected under water. Formerly, lime and iron were used to destroy the combination between the mercury and sulfur, but at present, this is accomplished with the oxygen of the air.

The mercury thus obtained is often separated from its impurities by mechanically stirring it in an iron bowl having a perforated bottom. The soot, containing some ash and traces of kerosene, is thrown out at the top of the bowl and the mercury runs through the holes in the bottom. The metallic impurities, *e. g.*, tin, lead, copper, zinc, silver, etc., may be eliminated by allowing the finely divided metal to drop through a column of nitric acid and mercury

nitrate. The mercury is then dried, pressed through chamois and distilled in vacuum from a glass retort.

**Pharmacological Action of Mercury.**—Mercury and its salts have several important uses in therapeutics. Practically all of the therapeutic applications may be looked upon as modifications of the principal action of the mercuric ion, *i. e.*, a protoplasmic poison. It is probably of more advantage to discuss them from this standpoint than from the action of specific chemical types such as metallic, mercuric and mercurous mercury. The most important therapeutic uses of mercury and its salts are (1) diuretic, (2) antiseptic, (3) antisyphilitic, (4) cathartic, (5) parasiticidal and fungicidal.

1. *Diuretic Action.*—The diuretic action of mercury salts, inorganic and organic, is probably due to a direct renal effect by mercuric ion. To obtain a diuretic effect the organic mercurials are used almost exclusively, *e. g.*, salyrgan, mercurin, mercupurin, etc. They are much less highly ionized than the inorganic mercurials and for this reason are less apt to cause undesirable toxic reactions. The chief use of mercurial diuretics is to rid the body of excess fluid in the case of cardiac edema. It should be emphasized that the mercury compounds are used simply as potent diuretics in these conditions and have no curative action whatsoever except that incidental to the diuretic action. It is interesting to note the synergistic action of acid-forming diuretic salts with mercurials. If salts which produce an acidosis are administered for two days prior to the use of the mercurial, it has been found that the sum total of the diuresis is usually greater than that which might be expected on an additive basis. Likewise, it has been found that salts which produce an alkalosis, *e. g.*, sodium bicarbonate, inhibit the action of the mercurial diuretics.

2. *Antiseptic Action.*—Mercury salts, both mercurous and mercuric, possess a pronounced antiseptic activity. The antiseptic action is due to the mercuric ion which is a protein precipitant, although it is difficult to explain on this basis the antiseptic activity of organic mercurials which are more effective than the more highly ionized inorganic compounds. In general, however, the protein precipitating action of the mercuric ion is the basis of the antiseptic action. It does not distinguish between bacterial and human protein and, therefore, is quite irritating when applied to the tissues. Its action is lowered by the very fact that it precipitates protein indiscriminately instead of being specific for bacterial protein. One might assume from the foregoing discussion that solutions of mercury salts would be excellent antiseptics for non-protein substances such as surgical instruments, etc. Their chief drawback in this application is that they corrode metals badly and therefore their use is limited.

Mercurous chloride, probably acting *via* slow liberation of mercuric ion, is an excellent antiseptic and is used widely in about a 30 per cent ointment. It is used almost exclusively in the prophylaxis of syphilis in the well-known Army and Navy prophylactics.

It is said that almost 100 per cent protection from syphilis is obtained by applying the ointment to the affected parts within an hour after exposure.

3. *Antisyphilitic Action.*—Mercury and its salts have been used since the end of the fifteenth century in the prophylaxis and treatment of syphilis. As previously indicated, calomel ointment is used as an efficient prophylactic. However, the use of mercurials in the treatment of syphilis has been largely superseded by more efficient medications, *e. g.*, arsenicals and bismuth compounds. One of the most used mercury preparations in this connection is an ointment of metallic mercury which is applied by inunction (rubbing into the skin). It is vigorously rubbed into the skin in areas where it is most readily absorbed, *e. g.*, armpits, groins, etc. In this form of medication, the metallic mercury is gradually changed into more or less soluble compounds by the body.

Although mercury compounds, intramuscularly and intravenously, have not been used extensively, constant research has gone on in an effort to minimize the difficulties accompanying this type of medication. Intramuscular usage is desirable from the standpoint of slowing down absorption so that less frequent injections are necessary. Some of the organic mercurials have become important in connection with intramuscular use.

The oral route of administration is occasionally resorted to in which case yellow mercurous iodide is the preparation of choice.

4. *Cathartic Action.*—Although this action is seldom used in modern therapy, at one time it was regarded as standard practice (see Mild Mercurous Chloride, p. 401). The laxative effect is undoubtedly a function of the irritant properties of the mercuric ion which is slowly liberated from the insoluble mercurous chloride, the salt that is used almost exclusively. The principal therapeutic advantage of this cathartic over most other cathartics is that its action starts high in the small intestine giving a thorough cleansing.

5. *Parasiticidal and Fungicidal Action.*—At one time, metallic mercury in the form of "blue ointment" (see p. 397) was used as an effective but untidy means of treating crab-louse infestation. It has been largely superseded by equally effective and more acceptable preparations. In the form of ammoniated mercury (see p. 399) ointment the effect of mercury is to act as an efficient antiseptic and fungicide, and is used largely in the treatment of impetigo contagiosa, ringworm infections, etc.

**Pharmaceutical Preparations and Uses.**—1. *Mercury* (Hydrargyrum, Quicksilver), U. S. P. XIII.—As previously pointed out, metallic mercury is used in the treatment of the secondary cutaneous lesions of syphilis. It is applied in the form of an ointment and rubbed into the skin. It is used in ointment form for the treatment of crab-louse infestation.

Aside from its medicinal uses, it is employed in the metallurgy of gold and silver. It is also used in making mercury compounds,

amalgams, thermometers, barometers, mirrors, vermillion and various physical and chemical apparatus.

2. *Mild Mercurial Ointment* (*Unguentum Hydrargyri Mite, Diluted Mercurial Ointment, Blue Ointment, Unguentum hydrargyri P. I.*), U. S. P. XIII.—“Mild Mercurial Ointment contains not less than 9 per cent and not more than 11 per cent of Hg.” It is prepared by incorporating 200 Gm. of Strong Mercurial Ointment (*q. v.*) with 800 Gm. of White Ointment. It is used for inunction and principally as a parasiticide.

3. *Strong Mercurial Ointment* (*Unguentum Hydrargyri Forte, Unguentum Hydrargyri, Mercurial Ointment*), U. S. P. XIII.—“Strong Mercurial Ointment contains not less than 47.5 and not more than 52.5 per cent of Hg.” This is prepared by extinguishing the mercury with Mercury Oleate and a portion of the fatty base consisting of wool fat, white wax, and white petrolatum. Another portion of the base is then added and triturated until the globules of mercury are no longer visible under a lens magnifying 10 diameters. The remainder of the wool-fat-petrolatum mixture is added and mixed thoroughly. It is the ointment of choice in the inunction treatment of syphilis, and the daily 4 Gm. dose is advantageously weighed for the patient on wax papers or in elastic capsules. It is also used in the preparation of Mild Mercurial Ointment (*q. v.*).

4. *Mercuric Nitrate Ointment* (*Unguentum Hydrargyri Nitratis, Citrine Ointment*), N. F. VIII.—This ointment “contains an amount of mercuric nitrate corresponding to not less than 6.65 per cent and not more than 7.35 per cent of Hg.” It is prepared by heating lard (free from water and consisting chiefly of glyceryl oleate) to about 45° C. and then adding part of the nitric acid all at once. The mixture is gently heated, holding an inverted funnel over the dish during the reaction, until the olein is converted into a yellow substance called *elaidin*, as evidenced by the rise of froth which accompanies the end reaction. It is then cooled and stirred to a bright citrine color. The mercury is dissolved in the remainder of the nitric acid (26), warmed to prevent crystallization, and mixed with the previously prepared lard. All contact with metals must be avoided.



*Elaidin* is a compound isomeric with the glyceryl ester of oleic acid  $[(\text{C}_{17}\text{H}_{33}\text{COO})_3\text{C}_3\text{H}_5]$ . It is the product formed by oxidizing oleic acid or oleates. Although the empirical formulæ for olein and elaidin are the same, the former melts at 14° C. and the latter at 45° C.

This ointment is used principally for the antiseptic action of mercuric nitrate (comparable to mercuric chloride). Its action is modified somewhat by being in the form of an ointment.

5. *Mercury Mass* (*Massa Hydrargyri, Blue Mass, Blue Pill*), N. F. VIII.—“Mercury Mass contains not less than 31 per cent and not more than 35 per cent of Hg.” The metallic mercury in

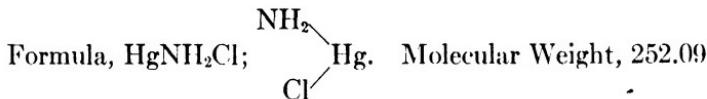
this preparation is extinguished with the aid of Mercury Oleate and Honey until it cannot be seen under a lens magnifying 10 diameters. Finally, the other ingredients (glycyrhiza, althea and glycerin) are incorporated to make a homogenous mass. The preparation is used as a cathartic which is said to cause less griping than calomel. Average dose—0.2 Gm. (approximately 3 grains).

6. *Mercury with Chalk* (*Hydrargyrum cum Creta*), N. F. VIII.— “Mercury with Chalk contains not less than 36 per cent and not more than 40 per cent of Hg.” The metallic mercury is extinguished by agitation with honey and, after mixing with prepared chalk, dried to a powder. It is used as a laxative and also (rarely) to obtain the constitutional effect of mercury in infantile syphilis. Average dose—0.25 Gm. (approximately 4 grains).

### OFFICIAL MERCURY COMPOUNDS

#### AMMONIATED MERCURY

*Ammoniated Mercury*, U. S. P. XIII



**Physical Properties.**—Ammoniated Mercury occurs in white, easily powdered pieces, or as a white, amorphous powder. It is odorless, and is stable in air, but is affected by light. It has a styptic, metallic taste. It is insoluble in water and in alcohol. By prolonged washing with water, the salt turns yellow due to the formation of a basic compound,  $\text{NH}_2(\text{Hg}_2\text{O})\text{Cl}$ . Warm hydrochloric, nitric, and acetic acids readily dissolve it. Below red heat, ammoniated mercury is decomposed without fusion, and at red heat it is volatilized.

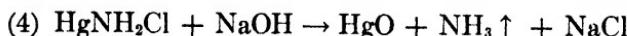
**Chemical Properties.**—As pointed out above, this compound decomposes without fusion (1) and when heated is sometimes known as “non-fusible white precipitate” to distinguish it from a related compound,  $\text{Hg}(\text{NH}_3)_2\text{Cl}_2$  (fusible white precipitate). The infusible form is converted to the fusible form by treating it with a hot ammonium chloride solution (2).



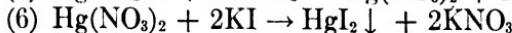
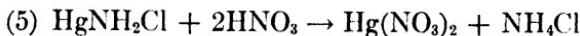
Prolonged washing of the compound with water results in the formation of a basic compound (3).



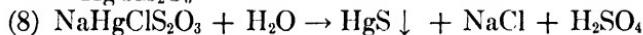
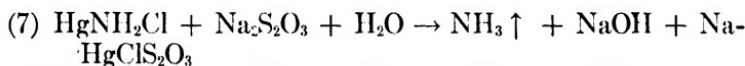
When the salt is heated with a solution of a fixed alkali hydroxide, yellow oxide of mercury is formed and ammonia is liberated (4).



When ammoniated mercury is dissolved in nitric acid (5) and the liquid treated with a solution of potassium iodide, a red precipitate of mercuric iodide (soluble in an excess of the precipitant) is formed (6).



A cold solution of ammonium carbonate, or a cold 50 per cent solution of sodium thiosulfate readily dissolves the salt (7) with the evolution of ammonia. When this solution is heated for a short time, red mercuric sulfide is precipitated and turns black on long boiling (8).



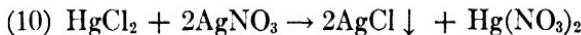
**Official Tests for Identity.**—1. One Gm. of the compound is soluble in a cold solution of 5 Gm. of  $\text{Na}_2\text{S}_2\text{O}_3$  in 5 cc. of water, evolving ammonia in the process (7).

2. When heated with sodium hydroxide T.S. the material becomes yellow due to formation of mercuric oxide and evolves ammonia (4).

3. A solution of ammoniated mercury in nitric acid (5) gives a red precipitate with potassium iodide T.S. (6). The precipitate is soluble in an excess of the reagent (9).



4. A solution of ammoniated mercury in nitric acid gives a precipitate with silver nitrate T.S. (10).



**Commercial Manufacture.**—A cold solution of mercuric chloride is poured slowly and with constant stirring into cold ammonia water (11). The solutions should be kept cold in order to minimize hydrolysis to basic compounds, as well as to prevent loss of ammonia. The precipitate is washed with very dilute ammonia water and finally dried in a dark place at a temperature not exceeding 30° C.



**Laboratory Preparation.**—Dissolve 12.5 Gm. of mercuric chloride in 200 cc. of warm distilled water. Filter and allow it to cool. Pour the filtrate gradually and with constant stirring into 20 cc. of ammonia water, taking care that the latter is in slight excess. Collect the precipitate upon a filter and wash it with two successive solutions of 5 cc. of ammonia water in 100 cc. of distilled water. Finally, dry the precipitate between sheets of bibulous paper in a dark place at a temperature not exceeding 30° C.

**Pharmaceutical Preparations and Uses.**—1. *Ammoniated Mercury* (*Hydrargyrum Ammoniatum*, White Precipitate), U. S. P. XIII.—“Ammoniated Mercury contains not less than 78 per cent and not

more than 80 per cent of Hg, corresponding to not less than 98 per cent of  $\text{HgNH}_2\text{Cl}$ ." This compound is occasionally used as a dusting powder against eczema and parasitic skin diseases. Usually it is applied in the form of an ointment (*q. v.*). It is considered to be a fairly efficient treatment for impetigo contagiosa. It might be mentioned here that the French *Précipité Blanc* (white precipitate) is calomel and *not* ammoniated mercury. Therefore, great care should be exercised in the interpretation of a French prescription so as not to confuse these compounds.

2. *Ammoniated Mercury Ointment* (*Unguentum Hydrargyri Ammoniati*, White Precipitate Ointment), U. S. P. XIII.—This ointment "contains an amount of ammoniated mercury corresponding to not less than 3.5 per cent and not more than 4.5 per cent of Hg." It is made by incorporating 5 per cent of ammoniated mercury into an ointment base consisting of 5 per cent wool fat and the remainder white ointment. This ointment has a fairly satisfactory skin-penetrating action which probably accounts in part for its activity. It is important to note that as late as the U. S. P. XI this ointment had a concentration of 10 per cent of ammoniated mercury and it is still obtainable in this concentration although the 5 per cent is the official form.

## ¶ MERCURIC CHLORIDE

### *Mercury Bichloride*, N. F. VIII

Formula,  $\text{HgCl}_2$ . Molecular Weight, 271.52

**Physical Properties.**—Mercuric Chloride crystallizes in white, odorless, rhombic prisms. It occurs also in the form of large crystalline masses, or as a white powder having a specific gravity of 5.44 at 20° C. Water hydrolyzes it, yielding a slightly acid solution which may be made neutral by the addition of sodium chloride. It is only feebly ionized. (In a normal solution at 18° C. only 0.01 per cent of  $\text{HgCl}_2$  is ionized.) (See p. 401.)

One Gm. of mercury bichloride dissolves in 13.5 cc. of water, in 3.8 cc. of alcohol, in about 12 cc. of glycerin, and in 25 cc. of ether, at 25° C. One Gm. dissolves in 2.1 cc. of boiling water and in 1.6 cc. of boiling alcohol.

At about 277° C. the salt fuses to a colorless liquid which boils at about 300° C. and gives off dense, white vapors of  $\text{HgCl}_2$ .

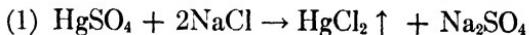
**Chemical Properties.**—The chemical properties of mercury bichloride are those of the mercuric ion (*q. v.*) and the chloride ion (*q. v.*).

**Official Tests for Identity.**—1. A 1 in 20 aqueous solution responds to the tests for *Mercuric Salts* (*q. v.*).

2. An aqueous solution also responds to all tests for *Chloride* (*q. v.*).

**Commercial Manufacture.**—1. Mercuric sulfate, made by heating mercury (4 parts) with sulfuric acid (5 parts) and drying, is thoroughly mixed with about one-half its weight of sodium chloride (1)

and a small amount of manganese dioxide (to prevent mercurous salt formation) and placed in clay or glass vessels. These are heated on a sand-bath until the bichloride sublimes as white, rhombic crystals into the upper part of the vessel. The container is broken and the salt purified, if necessary, by resublimation.



2. Mercuric chloride is also obtained by direct union of the elements. About 50 pounds of mercury are heated nearly to boiling in a large glass retort and subjected to the action of gaseous chlorine for from eight to ten hours. The bichloride that is formed sublimes and condenses on the cold, enlarged portion of the retort.

3. It is also made by dissolving mercuric oxide ( $\text{HgO}$ ) in hydrochloric acid and evaporating the solution. The product is usually purified by sublimation.

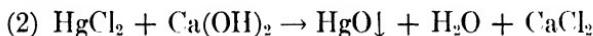
**Pharmaceutical Preparations and Uses.**—1. *Mercury Bichloride* (Hydrargyri Bichloridum, Corrosive Mercuric Chloride, Corrosive Sublimate, Mercuric Chloride), N. F. VIII.—Mercury Bichloride, when dried over sulfuric acid for eighteen hours, contains not less than 99.5 per cent of  $\text{HgCl}_2$ . The N. F. cautions: *Mercury Bichloride is extremely poisonous.* In aqueous solution, mercuric chloride ionizes only slightly and it polymerizes to form compounds such as  $(\text{HgCl}_2)_2$  and  $(\text{HgCl}_2)_3$ . However, the speed with which it replaces its ions makes its chemical behavior simulate a very highly ionized compound and therefore it is a very effective germicidal agent. It is used in concentrations of 1 to 1000 as a disinfectant hand wash. Proteins greatly lessen the activity of bichloride. Because of the irritant action of bichloride and also because of the toxic effects produced, its solutions are seldom used to irrigate wounds. It is used very little internally, if at all, although when so employed it will exert a diuretic effect.

2. *Mercury Bichloride Large Poison Tablets* (Toxitabellæ Hydrargyri Bichloridi Magnæ, Large Corrosive Sublimate Tablets, Large Bichloride Tablets), N. F. VIII.—These tablets "contain an average of not less than 0.42 Gm. and not more than 0.52 Gm. of  $\text{HgCl}_2$ , with a sufficient quantity of a suitable excipient or diluent."

In addition to approximately  $7\frac{1}{2}$  grains of Mercury Bichloride, they usually contain either sodium or ammonium chloride. These tablets must be of a distinctive color, not white; they must be of an angular or irregular shape, not discoid. When sold in small quantities suitable for household use, they must be dispensed in glass containers of a distinctive, angular shape, having irregular or roughened sides or edges. On the exterior of each container must be placed a red printed label bearing the word "POISON" and a statement indicating the amount of mercury bichloride in each tablet. One tablet dissolved in a pint of water makes approximately a 1 in 1000 solution. These tablets represent a convenient method for making a fairly accurate 1 to 1000 solution for disinfecting purposes.

3. *Mercury Bichloride Small Poison Tablets* (*Toxitabellæ Hydrargyri Bichloridi Parvæ*, Small Corrosive Sublimate Tablets, Small Bichloride Tablets), N. F. VIII.—These tablets contain an average of not less than 0.11 Gm. and not more than 0.14 Gm. of  $\text{HgCl}_2$ , with a sufficient quantity of a suitable excipient or diluent. These tablets contain approximately 2 grains of mercuric chloride and must conform to the specifications as to color, shape, containers used, labeling, etc., given for Mercury Bichloride Large Poison Tablets. One tablet dissolved in a pint of water makes approximately a 1 in 4000 solution.

4. *Yellow Lotion* (*Lotio Flava*, Yellow Wash), N. F. VIII.—This lotion is prepared by dissolving 3 Gm. of mercury bichloride in 35 cc. of boiling water. This solution is added with stirring to enough calcium hydroxide solution to make 1000 cc. The reaction that takes place is to form yellow mercuric oxide (2). The formation of a reddish-brown precipitate at the time of mixing the solutions may be due to a deficiency of calcium hydroxide in the lime water or to an excess of mercuric chloride. The precipitate is thought to be a mixture of basic compounds of mercury. This preparation should be freshly prepared because the fine precipitate has a tendency to coagulate into larger particles on standing for some time.



### MERCURIC CYANIDE

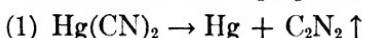
#### *Mercuric Cyanide*, N. F. VIII

Formula,  $\text{Hg}(\text{CN})_2$ . Molecular Weight, 252.65

**Physical Properties.**—This salt occurs as colorless or white, odorless, prismatic crystals, or as a white, odorless powder. Its aqueous solutions are neutral to litmus paper and it is affected by light.

One Gm. dissolves in about 13 cc. of water and about 13 cc. of alcohol at  $25^\circ\text{C}$ . One Gm. dissolves in about 3 cc. of boiling water and in about 6 cc. of boiling alcohol. It is sparingly soluble in ether.

**Chemical Properties.**—Mercuric cyanide is decomposed readily by simple heating to give metallic mercury and cyanogen gas (1). This reaction is used as a preparative method for making cyanogen.

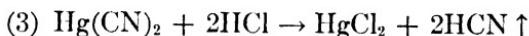


In solution, mercuric cyanide is not dissociated. This fact is borne out by its failure to conduct the electric current and by the fact that its molecular weight can be obtained by the freezing-point method. This is because it shows no abnormal depression of the freezing-point beyond that normally given by non-electrolytes (sugar, etc.) which is  $1.86^\circ\text{C}$ . in water. Because of the non-ionic character of its solutions it fails to give reactions characteristic of either the mercuric or cyanide ions.

Solutions of mercuric cyanide react with alkali cyanides to form new compounds. This is illustrated by the reaction of potassium cyanide with mercuric cyanide (2).



Acidification of solutions of mercuric cyanide results in the formation of hydrocyanic acid (3).



**Official Tests for Identity.**—1. When slowly heated in a test-tube, the salt decrepitates and decomposes into metallic mercury and inflammable cyanogen gas (1) which burns with a purple flame. On further heating the blackish residue of paracyanogen ( $\text{C}_2\text{N}_2$ )<sub>n</sub> is completely dissipated.

2. Gently heating a mixture of equal parts of mercuric cyanide and iodine in a test-tube causes at first the formation of a yellow sublimate of mercuric iodide which later turns yellow. Above this is a sublimate of colorless, needle-shaped crystals.

3. When a solution (1 in 20) is acidified with diluted hydrochloric acid, the characteristic odor of hydrocyanic acid (3) is evolved. Care should be exercised in breathing these vapors since they are extremely toxic.

**Commercial Manufacture.**—Mercuric Cyanide may be made by simply reacting yellow mercuric oxide with aqueous hydrocyanic acid (4).



It is also prepared by boiling Prussian blue ( $\text{Fe}_4(\text{Fe}(\text{CN})_6)_3$ ) with water and yellow mercuric oxide. In this reaction mercuric cyanide goes into solution and ferric oxide precipitates.

**Pharmaceutical Preparations and Uses.**—1. *Mercuric Cyanide* (Hydargyri Cyanidum), N. F. VIII.—“Mercuric Cyanide, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of  $\text{Hg}(\text{CN})_2$ .” The N. F. cautions: “*Because of the extremely poisonous nature of Mercuric Cyanide and of the gas evolved from it upon treatment with acids, all tests must be made in a hood, with a strong draft, and special care must be taken to avoid inhalation of fumes. Pipettes must not be used in measuring solutions of Mercuric Cyanide.*” Because mercuric cyanide does not precipitate protein it is much less irritating than mercuric chloride. It can be used locally as an antiseptic and can be applied to mucous membranes. It has also been suggested as a mercurial diuretic in cardiac edemas, although it is recommended that it be used only as a last resort after all other drugs have failed. It is contraindicated, as are all mercurials, in the presence of renal damage, and for that reason should not be used as a diuretic for renal edemas.

It has also been used as an antisyphilitic in the late stage of syphilis of the central nervous system, the heart, or liver where arsenicals are initially contraindicated.

In diphtheria and croup, mercuric cyanide is used in a 1 to 10,000 solution as a gargle, and, in fibrinous rhinitis, it is used on a tampon in a 1 to 2500 solution. Solutions of 1 to 4000 to 1 to 2000 may be used for application to the eye and mucous membranes.<sup>1</sup>

### MERCURIC IODIDE

*Red Mercuric Iodide*, N. F. VIII

Formula,  $HgI_2$ . Molecular Weight, 454.45

**Physical Properties.**—Mercuric Iodide occurs in two microcrystalline modifications, red (tetragonal octahedra, stable below 127° C. at 760 mm.) and yellow (rhombic prisms, stable above 127° C. at 760 mm.). Its specific gravity is 6.283 at 20° C.

Red mercuric iodide is practically insoluble in water. One Gm. of it dissolves in about 115 cc. of alcohol, in about 910 cc. of chloroform, or in about 120 cc. of ether, at 25° C., or in about 20 cc. of boiling alcohol. The salt dissolves in solutions of the soluble iodides, mercuric chloride, sodium thiosulfate, and in hot solutions of the alkali chlorides.

**Chemical Properties.**—Because of its insolubility, mercuric iodide enters into few chemical reactions. However, it is soluble in an excess of potassium iodide solution due to the formation of a complex salt (1). The same is also true of mercuric chloride solutions which dissolve mercuric iodide forming a soluble double salt (2).

- (1)  $HgI_2 + 2KI \rightarrow K_2HgI_4$  (soluble)
- (2)  $HgI_2 + 2HgCl_2 \rightarrow HgI_2 \cdot 2HgCl_2$  (soluble)

Similar considerations are responsible for the solubility of the salt in solutions of sodium thiosulfate and alkali chlorides.

It is interesting to note that the dissolving of mercuric iodide in potassium iodide solution produces a solution known as *Mayer's reagent* which is widely used as a testing agent for alkaloids because it readily precipitates most alkaloids from solution. If the Mayer's reagent is alkalized with potassium hydroxide, the resulting solution is known as *Nessler's reagent*. This reagent is used for the detection of small amounts of ammonia in water because it forms a yellow to brown coloration (depending on the concentration of  $NH_3$ ) in the solution.

**Official Tests for Identity.**—1. If about 0.1 Gm. of the salt is boiled with 2 cc. of sodium hydroxide T.S., filtered, and the filtrate strongly acidified with nitric acid, the iodide is oxidized to free iodine. This may be detected by adding a few drops of starch solution which turns deep blue in the presence of iodine.

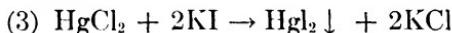
2. When heated to about 150° C. the red form changes to the yellow, but goes back to red on cooling. If heated to about 250° C. it fuses to a dark red liquid, which on cooling forms a yellow, crystalline mass. At about 350° C. it is volatilized. It is important

<sup>1</sup> J. Am. Pharm. Assn., Pr. Ed., p. 130 (March 1946).

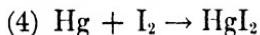
to note that the red form is the more stable of the two forms of mercuric iodide. The less stable is the yellow iodide which forms first in most cases, and which is converted rather quickly to the red form. Whenever the salt, either red or yellow, is volatilized it is always the yellow form which condenses out, and which is then converted to the red form.

3. If Red Mercuric Iodide is heated with potassium hydroxide T.S., and a little lactose added, metallic mercury is precipitated due to the reducing action of the lactose.

**Commercial Manufacture.**—1. Forty parts of mercuric chloride and 50 parts of potassium iodide are dissolved separately in sufficient amounts of water. The two solutions are poured simultaneously in thin streams into a large quantity of water that is well agitated (3). The resulting precipitate is thoroughly washed and dried in the dark between bibulous paper at a temperature not above 40° C. The product should be kept in amber colored bottles in a dark place.



2. Red iodide of mercury may be prepared by triturating in a mortar, 20 parts of mercury moistened with a little alcohol and 25.5 parts of iodine (4).



**Laboratory Preparation.**—Dissolve 8 Gm. of mercuric chloride and 10 Gm. of potassium iodide each in 80 cc. of distilled water and filter the solutions separately. Pour both solutions simultaneously and in a thin stream into 400 cc. of distilled water that is being agitated constantly. When the precipitate has subsided, decant the supernatant liquid, collect the precipitate on a filter and wash it with cold distilled water until the washings do not give more than a slight opalescence with silver nitrate test solution. Finally, dry in a dark place between sheets of absorbent paper at a temperature not exceeding 40° C.

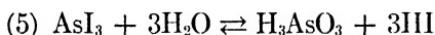
Particular care should be taken to avoid an excess of either member of the reaction mixture at any time during the operation, because an excess of mercuric chloride results in the formation of mercuric iodochloride ( $\text{HgI}_2 \cdot 2\text{HgCl}_2$  soluble) whereas an excess of potassium iodide forms potassium mercuric iodide ( $\text{K}_2\text{HgI}_4$  soluble). If the two solutions are mixed in the cold, the salt is precipitated as a fine red powder. If, on the other hand, the solutions are mixed while hot and then allowed to cool slowly, beautiful crystals may be obtained.

**Pharmaceutical Preparations and Uses.**—1. *Red Mercuric Iodide* (Hydrargyri Iodidum Rubrum, Mercuric Iodide), N. F. VIII.—Red Mercuric Iodide, when dried at 105° for three hours, contains not less than 99 per cent of  $\text{HgI}_2$ . This salt is a powerful irritant poison. Its action is similar to that of mercuric chloride and it is similarly used. It is used externally as a stimulant for

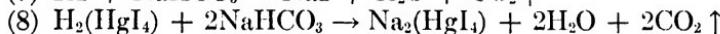
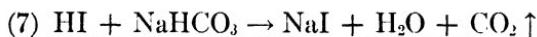
indolent ulcers, glandular swellings, etc. Average dose—4 mg. (approximately  $\frac{1}{6}$  grain).

2. *Red Mercuric Iodide Tablets* (*Tabellæ Hydrargyri Iodidi Rubri*), N. F. VIII.—These tablets "contain not less than 91 per cent and not more than 109 per cent of the labeled amount of  $HgI_2$ ." These tablets are usually available in 4, 8 and 15 mg. sizes for convenient administration orally whenever indicated. Average dose—4 mg. (approximately  $\frac{1}{6}$  grain) of Red Mercuric Iodide.

3. *Arsenic and Mercuric Iodides Solution* (*Liquor Arseni et Hydrargyri Iodidorum*, *Donovan's Solution*), N. F. VIII.—In the manufacture of this preparation 10 Gm. each of arsenic triiodide and red mercuric iodide, 9 Gm. of sodium bicarbonate and enough distilled water to make 1000 cc. of finished preparation are used. Some confusion seems to exist as to the exact reactions which take place between the two iodides (5, 6) and subsequently upon the addition of the sodium bicarbonate (7, 8). However, the following reactions have been suggested as taking place.<sup>1</sup>



The sodium bicarbonate then neutralizes the acids to form the sodium salts (7, 8).



The principal reason for the use of sodium bicarbonate is that the stability of the solution is greatly increased when the pH is adjusted between 6.5 and 7.5.<sup>2</sup> (See also p. 156.)

This preparation is used for the therapeutic effects of arsenic and mercury. It is not employed extensively but finds application in the treatment of certain skin diseases, chronic rheumatism and the later stages of syphilis. It is administered orally. Average dose—0.1 cc. (approximately  $1\frac{1}{2}$  minim).

### MERCURIC OXIDE

*Yellow Mercuric Oxide*, U. S. P. XIII

*Red Mercuric Oxide*, N. F. VIII

Formula,  $HgO$ . Molecular Weight, 216.61

**Physical Properties.**—1. *Yellow Mercuric Oxide*.—This oxide is a yellow to orange-yellow, heavy, impalpable powder which is odorless and stable in air. It is discolored on exposure to light. It is practically insoluble in water and in alcohol, but is readily soluble in diluted hydrochloric and nitric acids to form colorless solutions.

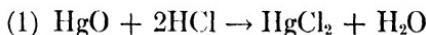
<sup>1</sup> Husa *et al.*: J. Am. Pharm. Assn., **19**, 328 (1930).

<sup>2</sup> Husa: J. Am. Pharm. Assn., **21**, 211, (1932).

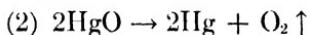
**2. Red Mercuric Oxide.**—This oxide occurs as heavy, orange-red crystalline scales, or as a crystalline powder. It acquires a yellow color when finely divided. It is odorless and has a slight metallic taste. It is affected by light. Its solubilities are the same as those of the yellow form.

Although the two forms given above have identical chemical formulæ, they have different colors; the difference in colors being ascribed to a difference in particle size (the red is coarse and the yellow is fine).

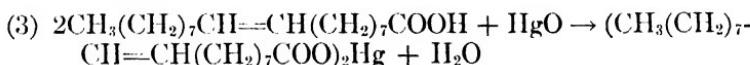
**Chemical Properties.**—Both of these oxides behave the same chemically. They are readily soluble in diluted acids, *e. g.*, hydrochloric acid (1).



When either of the oxides is heated to red heat, it is decomposed into oxygen and vapors of metallic mercury (2).



Mercuric oxide will react with oleic acid to form mercury oleate, a salt of an organic acid (3).



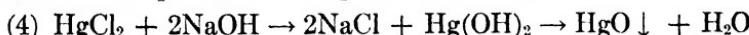
**Official Tests for Identity.**—1. *Yellow Mercuric Oxide.*—A solution of yellow mercuric oxide prepared by mixing 1 Gm. of the compound with 20 cc. of water and adding enough hydrochloric acid to just dissolve it (1) will give all tests for *Mercuric Compounds* (*q. v.*).

2. *Red Mercuric Oxide.*—*A.* When heated to approximately 400° C., this oxide takes on a dusky red-purple color, but goes back to the original red color on cooling.

*B.* A solution of the oxide in diluted nitric or hydrochloric acids responds to the tests for *Mercuric Compounds* (*q. v.*).

**Commercial Manufacture.**—1. *Yellow Mercuric Oxide.*—In the manufacture of yellow mercuric oxide, all of the operations are carried on in the dark, thereby insuring a bright orange-yellow product.

A concentrated solution of mercuric chloride is poured slowly and with constant agitation, into a dilute solution of sodium hydroxide free from carbonate (4). The mixture is allowed to stand at room temperature for approximately one hour in order to permit of complete decomposition and to allow the precipitate to settle. Then the supernatant liquid is poured off and the precipitate repeatedly washed with water until the washings are free from alkali. The yellow precipitate is drained and dried on absorbent paper, in a dark place, at a temperature of about 30° C.



2. *Red Mercuric Oxide.*—Despite the fact that this oxide of mercury is obtained by calcination and not by precipitation, it is

commonly called "*red precipitate*." It is usually prepared by triturating mercuric nitrate with metallic mercury until the latter completely disappears and then heating the mixture in a metallic capsule or in a small muffle furnace until fumes of nitrogen dioxide cease to be evolved (5).



The temperature at which the calcination is conducted must not be too great lest the mercuric oxide be decomposed into oxygen and vapors of metallic mercury.

**Laboratory Preparation.**—1. *Yellow Mercuric Oxide*.—Dissolve 25 Gm. of mercuric chloride in 250 cc. of warm distilled water and filter. Dissolve 10 Gm. of sodium hydroxide (free from carbonate) in 250 cc. of cold distilled water. Slowly pour the solution of mercuric chloride into the solution of the alkali, stirring it constantly. Allow the mixture to stand for about 1 hour at a temperature of about 30° C., stirring it frequently. Then decant the supernatant liquid from the precipitate and wash the latter repeatedly by affusion and decantation with separate portions of 250 cc. of distilled water. Collect the precipitate on a strainer and continue the washing with warm distilled water until a small portion of the washings do not give a yellow turbidity at the line of contact with a little mercuric chloride test solution. Allow the precipitate to drain and dry in a dark place between sheets of bibulous paper at a temperature not exceeding 30° C.

In the above, it is well to note that the solution of mercuric chloride must be poured into the solution of the alkali in order to avoid the precipitation of brown mercuric oxychloride.

2. *Red Mercuric Oxide*.—Dissolve 16 Gm. of mercury in 18 Gm. of nitric acid which previously has been diluted with 8 cc. of distilled water. Evaporate the solution to dryness. To the residue, add 16 Gm. of mercury and triturate in a mortar until metallic globules are no longer visible and the mixture appears to be uniform. Then heat this mixture in a porcelain dish over a sand bath under a hood, stirring it frequently, until acid vapors are no longer evolved. If the nitric acid is contaminated with hydrochloric acid, a corresponding amount of mercuric chloride and finally oxychloride will be formed, the latter remaining with the mercuric oxide. The last traces of acid may be removed by boiling the product with dilute sodium hydroxide and washing free from alkali.

**Pharmaceutical Preparations and Uses.**—1. *Yellow Mercuric Oxide* (*Hydrargyri Oxidum Flavum*, *Yellow Precipitate*), U. S. P. XIII.—“Yellow Mercuric Oxide, when dried at 110° to constant weight, contains not less than 99.5 per cent of HgO.” Because of its mild antiseptic effect, yellow oxide of mercury is used (mostly as an ointment) in ophthalmology for treating a number of inflammatory eye conditions.

2. *Yellow Mercuric Oxide Ointment* (*Unguentum Hydrargyri Oxidi Flavi*), U. S. P. XIII.—This ointment “contains not less than

0.9 per cent and not more than 1.1 per cent of HgO." It is made by incorporating 1 per cent of yellow mercuric oxide in a base composed of liquid petrolatum (1 per cent) and the remainder white ointment. It is obvious that the oxide must be in a fine state of subdivision since its principal use is for the eye. Because it is intended for ophthalmic use it is usually marketed in 1 or 2 dram ointment tubes having a smooth rounded tip to minimize traumatic danger.

3. *Mercury Oleate* (Oleatum Hydrargyri), U. S. P. XIII.—This oleate "contains the equivalent of not less than 24 per cent and not more than 26 per cent of HgO." This preparation is made by dissolving 25 Gm. of yellow mercuric oxide in sufficient oleic acid to make 100 Gm. of finished preparation. It is used to prepare Strong Mercurial Ointment and Mercury Mass.

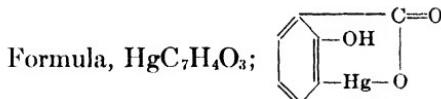
4. *Red Mercuric Oxide* (Hydrargyri Oxidum Rubrum, Red Precipitate), N. F. VIII.—Red Mercuric Oxide, when dried at 120° for three hours, contains not less than 99.5 per cent of HgO. Because of its grittiness it cannot be used in the eye. However, its mild antiseptic action recommends it in the form of an ointment for treating skin diseases.

5. *Red Mercuric Oxide Ointment* (Unguentum Hydrargyri Oxidi Rubri), N. F. VIII.—This ointment "contains not less than 9.5 per cent and not more than 10.5 per cent of HgO." It is prepared by incorporating 10 per cent of red mercuric oxide (in very fine powder) into a base composed of liquid petrolatum (5 per cent), yellow wax (5 per cent), wool fat (30 per cent) and petrolatum (50 per cent).

*Note.*—It is recommended by both the N. F. and U. S. P. that the respective ointments of mercuric oxide should *not* be allowed to come in contact with metallic utensils or containers other than those made of tin.

## MERCURIC SALICYLATE

### *Mercuric Salicylate*, N. F. VIII

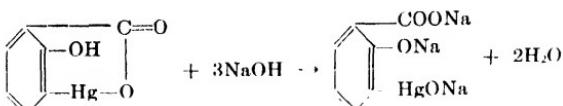


Molecular Weight, 336.71

**Physical Properties.**—Mercuric Salicylate occurs as a white, or slightly yellow or slightly pink, odorless powder. It is affected by light. Mercuric Salicylate is practically insoluble in water and in alcohol. It is dissolved by solutions of the fixed alkali hydroxides, by solutions of the alkali carbonates, and by solutions of alkali halides.

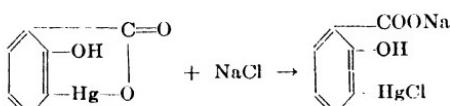
**Chemical Properties.**—Although this salt is practically insoluble in water it can be solubilized by alkali hydroxides, alkali carbonates and alkali halides. The reaction expressing the solubility in alkali hydroxides (1) and carbonates is best represented by the following:

(1)



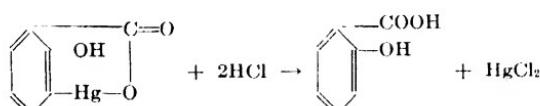
The solubility in alkali halides, *e. g.*, sodium chloride (2) is represented by

(2)



The salt is decomposed by hydrochloric acid into salicylic acid and mercuric chloride (3).

(3)

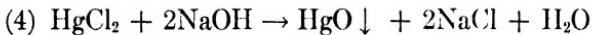


The salicylic acid is insoluble in a cool solution, but the neutralized (with ammonia) solution containing mercuric chloride gives the reactions of the mercuric ion.

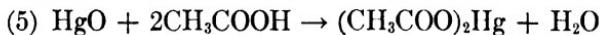
**Official Tests for Identity.**—1. One Gm. of the salt is heated with 25 cc. of hydrochloric acid (3) and the solution cooled. Salicylic acid separates out. The mixture is filtered, nearly neutralized with ammonia T.S. and copper foil immersed in it. A coating of metallic mercury forms on the foil. (See Tests for Mercuric Salts, p. 394.)

2. When 0.5 Gm. of Mercuric Salicylate is mixed with 10 cc. of distilled water, and a few drops of ferric chloride T.S. added, the mixture acquires a reddish-purple color due probably to the formation of ferric salicylate.

**Commercial Manufacture.**—Precipitated mercuric oxide is prepared by adding a solution of mercuric chloride to a solution of sodium hydroxide (4). The washed mercuric oxide is suspended

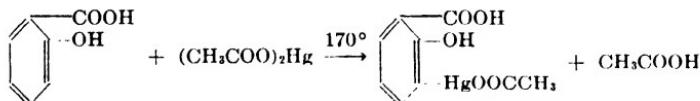


in water, salicylic acid and a little acetic acid added and the mixture heated until it becomes white. The reactions that take place are probably the conversion of mercuric oxide to mercuric acetate (5).

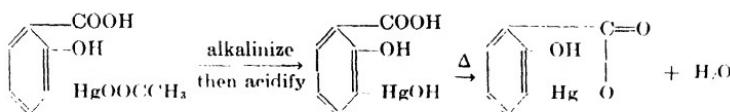


This then reacts as a mercurating agent upon the salicylic acid to form an intermediate which, upon alkalization, followed by acidification and heating, yields the desired compound (6, 7).

(6)



(7)

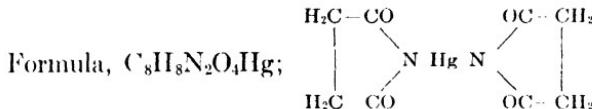


**Pharmaceutical Preparations and Uses.**—1. *Mercuric Salicylate* (Hydrargyri Salicylas), N. F. VIII.—“Mercuric Salicylate contains not less than 54 per cent and not more than 59.5 per cent of Hg.” This compound is very slightly ionized and, therefore, does not have the corrosive action of the more highly ionized compounds. It is one of the most popular of the mercury salts when suspended in oil for intramuscular injection in the treatment of syphilis. Injections are given once a week and are said to be quite painful. Average dose—Intramuscular, in oil, 0.1 Gm. (approximately 1½ grains).

2. *Mercuric Salicylate Ampuls* (Ampullæ Hydrargyri Salicylatis, Mercuric Salicylate Injection), N. F. VIII.—These ampuls “contain a sterile suspension of mercuric salicylate in a suitable fixed oil, and yield an amount of Hg equivalent to not less than 52.5 per cent and not more than 61 per cent of the labeled amount of  $HgC_7H_4O_3$ .” Average dose—Intramuscular, 0.1 Gm. (approximately 1½ grains) of Mercuric Salicylate.

### MERCURIC SUCCINIMIDE

#### *Mercuric Succinimide*, N. F. VIII



Molecular Weight, 396.77

**Physical Properties.**—Mercuric Succinimide occurs as small, white crystals, or as a white powder. It is odorless and is stable in air, but darkens on exposure to light. One Gm. of Mercuric Succinimide dissolves in 20 cc. of water at 25° C., and in about 5 cc. of boiling water. It is slightly soluble in alcohol and is insoluble in ether.

**Official Tests for Identity.**—1. The addition of sodium hydroxide T.S. to an aqueous solution of Mercuric Succinimide (1 in 25) produces a yellowish-white precipitate which is reduced to metallic mercury when the mixture is heated.

2. Add potassium iodide T.S., drop by drop, to a solution of Mercuric Succinimide (1 in 25). A yellow precipitate is produced which dissolves on the addition of an excess of the reagent.

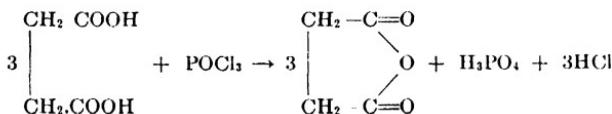
3. Heated with about five times its weight of zinc dust, Mercuric Succinimide evolves pyrrol, which imparts a red color to a pine shaving moistened with hydrochloric acid and held in the vapor.

4. Disperse about 0.5 Gm. of finely powdered Mercuric Succinimide in 50 cc. of cold ether in a flask, and pass hydrogen sulfide

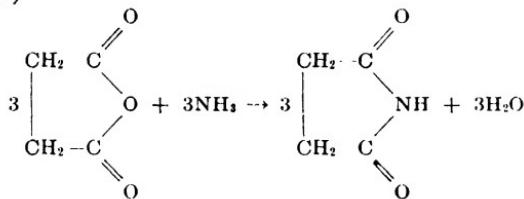
through the mixture until it has a distinct odor of hydrogen sulfide. A black precipitate of mercuric sulfide is produced. Filter the mixture, evaporate the clear filtrate to dryness, and dry for one hour at 100° C.; the residue of succinimide melts between 123° and 125° C.

**Commercial Manufacture.**—First, succinic anhydride is prepared by heating succinic acid with phosphorus oxychloride (or some other dehydrating agent) for some time and then distilling the anhydride (1). By heating the anhydride in a current of dry ammonia, the succinimide is produced (2). When freshly precipitated mercuric oxide and an aqueous solution of succinimide are heated together, mercuric succinimide is formed (3). The solution is filtered and evaporated to crystallization.

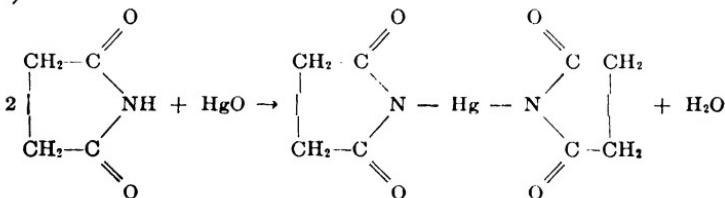
(1)



(2)



(3)



**Pharmaceutical Preparations and Uses.**—1. *Mercuric Succinimide* (Hydrargyri Succinimidum), N. F. VIII.—Mercuric Succinimide, when dried over sulfuric acid for eighteen hours, contains not less than 49.5 per cent and not more than 51 per cent of Hg, corresponding to not less than 98 per cent of  $\text{C}_8\text{H}_8\text{N}_2\text{O}_4\text{Hg}$ . This salt is used in the treatment of syphilis. It is of particular value when it is desired to rapidly mercurialize a patient. Its value as an intramuscular injection for maintenance of the mercury effect is hindered by the fact that it is water-soluble and injections must be made daily or every other day for satisfactory results. It may also be given orally in doses of from 10 to 15 mg., although it is usually administered intramuscularly in approximately the same dose. Average dose—Intramuscular, 15 mg. (approximately  $\frac{1}{4}$  grain).

2. *Mercuric Succinimide Ampuls* (Ampullæ Hydrargyri Succinimi, Mercuric Succinimide Injection), N. F. VIII.—These ampuls "contain a sterile solution of mercuric succinimide in water for injection, and yield an amount of Hg, equal to not less than 48 per cent and not more than 52 per cent of the labeled amount of C<sub>8</sub>H<sub>8</sub>-N<sub>2</sub>O<sub>4</sub>Hg." These ampuls are used for intramuscular injections of mercuric succinimide. Average dose—15 mg. of Mercuric Succinimide.

### MERCUROUS CHLORIDE

*Mild Mercurous Chloride*, U. S. P. XIII

Formula, HgCl. Molecular Weight, 236.07

**Physical Properties.**—Mercurous Chloride is a heavy, white, impalpable powder that is insoluble in water, in alcohol, in ether, and in cold dilute acids. The salt is odorless and tasteless. It is permanent in air, but turns slightly gray when exposed to light, due to decomposition into mercury and mercuric chloride. When triturated with strong pressure, it becomes yellowish-white. It is insoluble in water, in alcohol, in ether, and in cold dilute acids.

**Chemical Properties.**—When heated to about 383° C., mercurous chloride is converted into a vapor having a density that corresponds to the formula, HgCl. However, at this temperature, mercurous chloride is decomposed into mercuric chloride and mercury, which recombine in the cold and, therefore, the constitutional formula of calomel is thought to be Hg<sub>2</sub>Cl<sub>2</sub>.

Since mercurous chloride is insoluble in water it does not undergo very many chemical reactions. It does, however, react with lime water (see p. 330) (1), solutions of alkali hydroxides and ammonia water (2) to give a black precipitate.

- (1)  $\text{Hg}_2\text{Cl}_2 + \text{Ca}(\text{OH})_2 \rightarrow \text{Hg}_2(\text{OH})_2 \downarrow + \text{CaCl}_2$   
 $\text{Hg}_2(\text{OH})_2 \rightarrow \text{Hg}_2\text{O} + \text{H}_2\text{O}$
- (2)  $\text{Hg}_2\text{Cl}_2 + 2\text{NH}_4\text{OH} \rightarrow \text{HgNH}_2\text{Cl} \downarrow + \text{Hg} \downarrow + \text{NH}_4\text{Cl} + 2\text{H}_2\text{O}$

When a mixture of equal parts by weight of mercurous chloride and reagent anhydrous sodium carbonate (chloride-free) is heated in a dry test-tube, metallic mercury sublimes and forms a gray mirror on the inner surface of the cold parts of the tube (3).

- (3)  $2\text{Hg}_2\text{Cl}_2 + 2\text{Na}_2\text{CO}_3 \rightarrow 4\text{NaCl} + 2\text{Hg}_2\text{CO}_3$   
 $2\text{Hg}_2\text{CO}_3 \rightarrow 2\text{Hg}_2\text{O} + 2\text{CO}_2 \uparrow$   
 $2\text{Hg}_2\text{O} \rightarrow 4\text{Hg} \uparrow + \text{O}_2 \uparrow$

This decomposition is true of all compounds of mercury when heated with sodium carbonate.

By heating under the proper conditions mercurous chloride is decomposed to metallic mercury and poisonous mercuric chloride (4).

- (4)  $\text{Hg}_2\text{Cl}_2 \rightarrow \text{HgCl}_2 + \text{Hg}$

Light has a similar action to heat, decomposing the salt to mercuric chloride and mercury.

Mercurous chloride, in the solid form, is capable of absorbing ammonia gas to form a diammoniate (5).

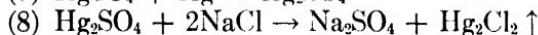
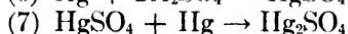


**Official Tests for Identity.**—1. Mild mercurous chloride is blackened by contact with calcium hydroxide T.S. (1), with solutions of alkali hydroxides, or with ammonia T.S. (2).

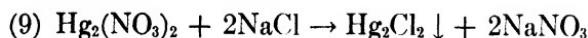
2. It decomposes to yield free mercury when heated in a test-tube, with an equal weight of anhydrous sodium carbonate (3). The mercury condenses on the wall of the tube. When the residue in the tube is treated with nitric acid, filtered, and silver nitrate added to the filtrate a white, curdy precipitate of silver chloride is formed showing the presence of the chloride ion.

**Commercial Manufacture.**—1. Mercurous chloride is usually prepared by heating a mixture of mercurous sulfate and sodium chloride and condensing the vapors of mercurous chloride that result. A mixture of sulfuric acid and mercury are heated together until a dry salt is obtained (6). A quantity of mercury sufficient to convert the mercuric sulfate into mercurous sulfate is then extinguished in the dried salt (7) and the product intimately mixed with the necessary amount of sodium chloride. The mixture is then sublimed and the vapors condensed in such a manner as to produce a fine, amorphous product (8). This is done by mixing the vapors of mercurous chloride with steam or cold air just as they enter the condensing chamber.

The impure product thus obtained is thoroughly agitated and washed with water to remove any mercuric chloride. It is then washed repeatedly with dilute nitric acid to dissolve any unchanged mercury and, after removing all traces of nitric acid, the salt is finally resublimed.



2. Mercurous chloride may also be made by adding a solution containing the chloride ion to any soluble mercurous salt (9). This method is used in making the *Précipité Blanc* (white precipitate) of the French Codex. (See Ammoniated Mercury, p. 400.) The product is more active than that made by sublimation and hence is usually given in doses about one-third of the pharmaceutical product. The greater activity is probably due to smaller particle size, which causes a greater surface to be exposed for a given weight of compound.



3. A technical grade of mercurous chloride is made by subliming an intimate mixture of mercuric chloride and the equivalent amount of mercury, or by passing sulfur dioxide into a solution of mercuric chloride.

**Pharmaceutical Preparations and Uses.**—1. *Mild Mercurous Chloride* (*Hydrargyri Chloridum Mite*, *Mercurous Chloride*, *Calomel*, *Subchloride of Mercury*), U. S. P. XIII.—Mild Mercurous Chloride, when dried over sulfuric acid for five hours, contains not less than 99.6 per cent of  $\text{HgCl}_2$ . The principal use of calomel is as a cathartic. It is insoluble in the gastric juice and is not absorbed from the stomach or rectum. It is attacked in the intestines by the alkaline pancreatic and intestinal juices and is slowly dissociated into mercury and yellow mercuric oxide; the latter dissolving slowly and incompletely in the intestinal fluid. The cathartic action is generally attributed to the irritant action of very small quantities of mercuric ion. For maximum cathartic effect from a given dose, it is desirable to give the dose in several portions spaced at twenty to thirty minute intervals. This spreads the irritant effect over a longer portion of the intestine than would otherwise be affected by the same dose given at one time. Because of the possibility of mercury poisoning, it is always advisable to follow the administration of calomel by a saline cathartic within six hours. Calomel enjoyed a widespread popularity at one time because it was thought to stimulate the flow of bile. This belief was based upon the fact that the stools were colored green and that this color was due to excessive bile secretion. The green coloration, however, has been shown to be due to the antiseptic effect of the mercury which prevents the normal conversion of biliverdin (green) to bilirubin by intestinal bacteria. There are very few instances in which the use of calomel is indicated as a cathartic. The very fact that a saline cathartic is required to remove it from the intestine, complicates its use.

Much more rational and based on a firmer scientific basis is the use of calomel in an ointment as a prophylactic against syphilis (see p. 395). For maximum antiseptic effect it is desirable to have the calomel in as fine a state of subdivision as possible. Average dose—0.12 Gm. (approximately 2 grains).

2. *Black Lotion* (*Lotio Nigra*, *Black Wash*, *Aqua Phagedænica Nigra*), N. F. VIII.—Mild mercurous chloride (9 Gm.) and acacia (1 Gm.) are triturated in a mortar. Water (100 cc.) is gradually added and the mixture is slowly added with constant stirring to enough calcium hydroxide solution to make 1000 cc. (See also p. 330.) The mixture should be freshly prepared because it has a tendency to form larger particles on standing. It is used as an antiseptic wash.

3. *Mild Mercurous Chloride and Sodium Bicarbonate Tablets* (*Tabellæ Hydrargyri Chloridi Mitis et Sodii Bicarbonatis*, *Calomel and Soda Tablets*), N. F. VIII.—These tablets "contain not less

than 92.5 per cent and not more than 107.5 per cent of the labeled amount of HgCl for tablets containing more than 15 mg., and not less than 90 per cent and not more than 110 per cent for tablets containing 15 mg. or less of HgCl." These tablets are used for the characteristic cathartic action of calomel. The use of sodium bicarbonate in these tablets has not been well-explained. Possibly it may be rationalized by the fact that it produces a "spot" alkalinity which would tend toward a more rapid mercuric oxide-protein combination with resultant increased peristalsis. There is also the possibility that the sodium chloride formed by the action of the hydrochloric acid of the stomach upon the bicarbonate tends toward the formation of some soluble bichloride<sup>1</sup> with resulting increased irritation.

4. *Mild Mercurous Chloride Ointment* (*Unguentum Hydrargyri Chloridi Mitis, Calomel Ointment*), N. F. VIII.—This ointment "contains not less than 28.5 per cent and not more than 31.5 per cent of HgCl." It is prepared by incorporating 30 per cent of Mild Mercurous Chloride in an ointment base composed of equal parts of hydrous wool fat and white petrolatum. It is used for the anti-septic effect of calomel.

5. *Compound Mild Mercurous Chloride Pills* (*Pilulae Hydrargyri Chloridi Mitis Composite, Compound Cathartic Pills*), N. F. VIII.—Compound colocynth extract, jalap resin, and gamboge are intimately mixed with calomel and massed with diluted alcohol. The mass is divided and rolled into pills. One pill contains 60 mg. of calomel and varying quantities of the other cathartic ingredients. The pills are commonly known as "C.C." pills. Average dose—2 pills.

6. *Mild Mercurous Chloride Tablets* (*Tabellæ Hydrargyri Chloridi Mitis, Calomel Tablets*), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of HgCl." They are used as a convenient form for administering calomel and are usually supplied in 6, 15, 30 and 60 mg. sizes. Average dose—60 mg. (approximately 1 grain) of Mild Mercurous Chloride, in tablets usually containing a fraction of the average dose.

7. *Santonin and Mild Mercurous Chloride Tablets* (*Tabellæ Santonini et Hydrargyri Chloridi Mitis, Santonin and Calomel Tablets*), N. F. VIII.—These tablets "contain not less than 92.5 per cent and not more than 107.5 per cent of the labeled amount of C<sub>15</sub>H<sub>18</sub>O<sub>3</sub> and of HgCl." These tablets are used for the anthelmintic action of santonin combined with the cathartic action of calomel to remove the dead and stunned intestinal worms. The tablets are usually marketed in sizes containing the following amounts of santonin and mild mercurous chloride: of each, 15, 30 and 60 mg. Average dose—60 mg. (approximately 1 grain) of Santonin; 0.12 Gm. (approximately 2 grains) of Mild Mercurous Chloride.

<sup>1</sup> Principles of Pharmacy—Arny (1911).

**MERCURIOUS IODIDE***Yellow Mercurous Iodide, N. F. VIII*Formula,  $\text{HgI}_2$ . Molecular Weight, 327.53

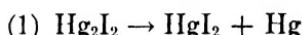
**Physical Properties.**—This salt occurs as a bright yellow, odorless and tasteless, amorphous powder. It decomposes upon exposure to light. It has a specific gravity of 7.70 at 20° C.

It is practically insoluble in water, and is insoluble in alcohol and in ether.

**Chemical Properties.**—It is decomposed by light into mercury and mercuric iodide (1) with the development of a greenish color which deepens as the amount of metallic mercury produced by the decomposition increases. Mercury in a finely divided state is blue in color, hence as the per cent of blue increases in the blue-yellow admixture the resultant green color becomes darker.

The salt is nearly insoluble in water. It is completely insoluble in alcohol or ether.

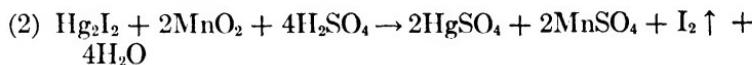
When carefully heated, the salt gradually acquires a red color but becomes yellow on cooling. When exposed to high temperatures (290° C. plus) it decomposes into mercury and mercuric iodide (1) which are finally volatilized.



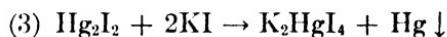
The reason for the use of the formula ( $\text{Hg}_2^{++}$ ) showing the bivalent mercurous form is the same as for mercurous chloride (see p. 413).

Mercurous iodide is decomposed by heating with sodium carbonate in exactly the same manner as mercurous chloride (see p. 413).

Heating the salt with sulfuric acid and a little manganese dioxide results in the formation of iodine (2).



Potassium iodide dissolves mercurous iodide and leaves a deposit of metallic mercury (3).



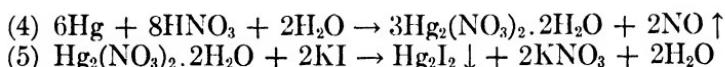
**Official Tests for Identity.**—1. Yellow Mercurous Iodide is blackened by ammonia T.S. or by sodium hydroxide T.S. in the same manner as mercurous chloride.

2. When the salt is heated with sulfuric acid and a little manganese dioxide, it evolves iodine vapors (2).

3. The addition of 0.5 Gm. of the salt to 10 cc. of potassium iodide T.S. results in the solution of the mercurous iodide together with the deposition of metallic mercury (3).

**Commercial Manufacture.**—The preparation of mercurous iodide is based upon a reaction between mercurous nitrate and potassium iodide. First, mercurous nitrate is made by treating a slight

excess of mercury with diluted nitric acid in a dark place (4). The crystals ( $\text{Hg}_2(\text{NO}_3)_2 \cdot 2\text{H}_2\text{O}$ ) are drained and then dried on absorbent paper in the dark. A weighed quantity of this salt is then dissolved in distilled water acidulated with nitric acid and a solution of the calculated amount of potassium iodide is added slowly and with constant stirring (5). The yellow precipitate is washed repeatedly until the washings do not give a test for nitrate ion and then dried at a temperature not exceeding 40° C. on bibulous paper, in the dark.



In the process described above, it is important that the solution of potassium iodide be *added to* the solution of mercurous nitrate. This order of mixing prevents the possible formation of some metallic mercury and mercuric iodide by the action of excess alkali iodide upon the freshly precipitated mercurous iodide. The mercuric iodide so formed reacts with the excess potassium iodide (6) to form potassium mercuric iodide, which is washed out of the precipitate of yellow iodide and lost, thus occasioning a low yield of the latter.



Yellow iodide of mercury is easily decomposed by light, hence the drying processes are conducted in the dark. Because mercurous nitrate is hydrolyzed so readily by water (see p. 392) to form an insoluble basic nitrate, nitric acid is added to prevent hydrolysis and thus effect a clear solution.

**Laboratory Preparation.**—Mix 4 cc. each of nitric acid and distilled water and, when the liquid is cool, pour it upon 10 Gm. of mercury contained in a small flask. Set the mixture aside in a cool, dark place (do not stopper the flask) and agitate it occasionally until the reaction ceases and a little mercury remains undissolved. Separate the crystals of mercurous nitrate which will have formed and allow them to drain in a funnel. Then dry them on bibulous paper in a dark place.

When the salt is dry, weigh 8 Gm. of it and dissolve in 130 cc. of distilled water to which 1.2 cc. of nitric acid has been added. Having previously prepared a solution of 3.2 Gm. of potassium iodide in 6.3 cc. of water, slowly pour the same into the solution of mercurous nitrate, constantly stirring the latter. Stir for fifteen minutes, allow the precipitate to subside, decant the supernatant liquid and wash the precipitate by decantation with 10 successive portions of 100 cc. of distilled water. Finally, transfer the precipitate to a filter and dry it in a dark place at a temperature not exceeding 40° C. between sheets of bibulous paper.

For explanation of process, see Commercial Manufacture (p. 417).

**Pharmaceutical Preparations and Uses.**—1. *Yellow Mercurous Iodide* (Hydrargyri Iodidum Flavum, Mercurous Iodide), N. F.

VIII.—Yellow Mercurous Iodide, when dried over sulfuric acid for four hours, contains not less than 99 per cent of HgI. This is possibly the best mercury salt for *oral* administration in the treatment of syphilis. However, it is used only to a very limited extent. It was introduced into medical practice in the early nineteenth century by Ricord and used extensively at a later date by his celebrated pupil, Fournier. Average dose—10mg. (approximately  $\frac{1}{6}$  grain).

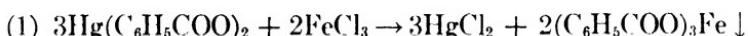
2. *Yellow Mercurous Iodide Tablets* (*Tabellæ Hydrargyri Iodidi Flavi, Mercurous Iodide Tablets*), N. F. VIII.—These tablets "contain not less than 91 per cent and not more than 109 per cent of the labeled amount of HgI." They are usually marketed in 8, 10, 15 and 30 mg. sizes. They are a convenient form for administering mercurous iodide orally. Average dose—10 mg. (approximately  $\frac{1}{6}$  grain) of Yellow Mercurous Iodide.

#### NON-OFFICIAL MERCURY COMPOUNDS

**Mercuric Benzoate** (*Hydrargyri Benzoas, Hydrargyrum Benzoinum*), N. N. R. (1947).—Formula  $Hg(C_6H_5COO)_2$ , Molecular Weight, 442.83. This salt of benzoic acid is a white, crystalline powder. It dissolves slightly in water to give a weakly acidic solution. It is more soluble in aqueous sodium chloride solution. It is insoluble in alcohol and in ether.

At 20° C. a 10 per cent solution of sodium benzoate will dissolve 1 per cent of its weight of mercuric benzoate. Alcohol decomposes mercuric benzoate to form a yellow basic salt.

Mercuric benzoate when dissolved with the aid of sodium chloride gives a black precipitate of mercuric sulfide when treated with hydrogen sulfide. A solution of mercuric benzoate effected in the manner described gives a precipitate of ferric benzoate with ferric chloride T.S. (1).



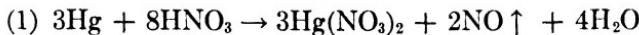
This salt is used for intramuscular injections in syphilis and locally in the treatment of gonorrhea. It has been largely replaced, however, by the organic mercurials.

**Mercuric Nitrate.**—Formula (anhydrous)  $Hg(NO_3)_2$ , Molecular Weight, 324.63. This salt occurs in the form of colorless crystals or as a white deliquescent powder. It is poisonous. It is soluble in water acidulated with nitric acid but is insoluble in alcohol. Its solutions are readily changed by hydrolysis into basic salts such as  $Hg(NO_3)_2 \cdot 0.5H_2O$ . Solutions of it are acid to litmus paper.

Being a readily ionizable compound, its solutions give reactions for the mercuric ion (*q. v.*) and the nitrate ion (*q. v.*).

It is prepared by treating mercury with an excess of boiling nitric acid. When reaction has ceased, the solution is allowed to cool,

whereupon crystals of the octahydrate ( $\text{Hg}(\text{NO}_3)_2 \cdot 8\text{H}_2\text{O}$ ) settle out (1). The product is purified by recrystallization.



This salt is highly irritating because its solutions contain the free mercuric ion to such a large extent. Its uses are the same as those of mercuric chloride. It is present in *Mercuric Nitrate Ointment*, N. F. VIII. (See p. 397.)

**Mercuric Oxycyanide** (*Hydrargyri Oxycyanidum*, *Hydrargyrum Oxycyanatum*, *Mercury Oxycyanide*), N. N. R. (1947).—Formula  $\text{Hg}(\text{CN})_2\text{HgO}$ , Molecular Weight, 469.26. This basic mercuric salt of hydrocyanic acid occurs as a white or nearly white, microcrystalline powder, soluble in about 80 parts of water, yielding a solution alkaline to litmus.

A saturated solution of the salt yields (1) a white precipitate with ammonium chloride, the precipitate being soluble in an excess of the reagent; (2) hydrogen sulfide gives a black precipitate of mercuric sulfide; and (3) potassium iodide solution precipitates red mercuric iodide, soluble in an excess of the reagent.

This salt is claimed to be less irritating than mercuric chloride and to have superior antiseptic power. In addition it is said not to corrode steel instruments.

It can be administered in the same doses as mercuric chloride and for topical application it can be used in 1 to 5000 solutions or even stronger.

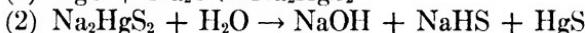
**Mercuric Sulfate**.—Formula  $\text{HgSO}_4$ , Molecular Weight, 296.67. Mercuric sulfate ( $\text{HgSO}_4$ ) exists as a heavy, white, crystalline (rhombic) anhydrous salt and as colorless, shining prisms or scales of the monohydrate ( $\text{HgSO}_4 \cdot \text{H}_2\text{O}$ ). At red heat, it is decomposed into mercury, oxygen, sulfur dioxide, and some mercurous sulfate. Finally, it is completely volatilized. Both the anhydrous and crystalline forms are readily hydrolyzed by water, yielding a yellow basic salt ( $\text{HgSO}_4 \cdot 2\text{HgO}$ ) called *turpeth* or *turpeth mineral*.

Mercuric sulfate can be made by heating in a flask on a sand-bath, 18 parts of mercury, 10 parts of concentrated sulfuric acid, 3 parts of water and 4 parts of 25 per cent nitric acid, until the evolution of nitrogen tetroxide ceases. Then the liquid is poured into an evaporating dish and evaporated to dryness.

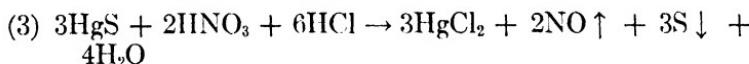
Mercuric sulfate is used in the preparation of mercuric chloride, calomel and turpeth mineral (*q. v.*), for filling galvanic batteries, as a catalyst, and as a reagent. This salt was never used in medicine. Turpeth mineral ( $\text{HgSO}_4 \cdot 2\text{HgO}$ ), however, was formerly official (U. S. P. 1890) as *Hydrargyri Subsulphas flavus* and was used in small doses as an alterative and in large doses as an emetic. Poisonous doses produced the same effects as corrosive sublimate.

**Mercuric Sulfide**.—Formula  $\text{HgS}$ , Molecular Weight, 232.67. Mercuric sulfide ( $\text{HgS}$ ), crystalline, is found in Nature as the red mineral *cinnabar*. It is formed as a black amorphous precipitate

when hydrogen sulfide is passed into a solution of a mercuric salt. The precipitate first formed is white ( $Hg_3Cl_2S_2$ ) but rapidly changes to yellow, then brown and finally black. These intermediate compounds are thought to be unstable thiochloride forms of mercuric mercury. If the black sulfide is digested at about  $45^\circ C.$  with an alkali sulfide, there is formed a product which easily hydrolyzes to mercuric sulfide (Vermilion, Artificial Cinnabar, Chinese Red, etc.), sodium hydroxide and sodium hydrosulfide (1 and 2).

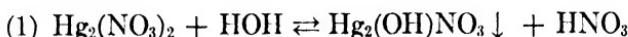


*Vermilion* is manufactured on a large scale by subliming a mixture of mercury and sulfur. The sublimate is levigated and then forms a bright scarlet red, odorless and tasteless powder. It is insoluble in water, alcohol, ether, and dilute acids. It dissolves slowly in hot concentrated hydrochloric acid. Hot concentrated nitric acid changes it into a white compound having a formula,  $Hg_3S_2(NO_3)_2$ . It is readily acted upon by even cold nitrohydrochloric acid (3) with the separation of sulfur.



In the form of lotions and ointments, mercuric sulfide has attained some measure of popularity as an antiseptic for treating various skin diseases. A colloidal mercury sulfide solution (N. N. R., 1947) consisting of 2 per cent of mercuric sulfide in water, stabilized with a hydrolyzed protein substance and preserved with 0.2 per cent of tricresol has been advocated for intramuscular use in the treatment of syphilis.

**Mercurous Nitrate.**—Formula (anhydrous)  $Hg_2(NO_3)_2$ , (crystals)  $Hg_2(NO_3)_2 \cdot 2H_2O$ , Molecular Weight, 561.26. Mercurous Nitrate is a colorless, white or slightly yellowish salt having a metallic taste. It forms monoclinic crystals of the dihydrate, which effloresce on exposure to air. It dissolves in 2 parts of warm water and gives an acid solution. The salt is hydrolyzed by water to form an insoluble basic nitrate (1), hence the use of nitric acid to effect a clear solution.

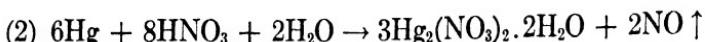


Mercurous nitrate is easily oxidized even by the atmosphere to mercuric nitrate, hence a little free mercury is kept in a solution in order to reduce to mercurous nitrate any mercuric nitrate that may be formed.

Solutions of mercurous nitrate possess all reactions for mercurous ion (see p. 392) and for nitrate ion (see p. 120).

To prepare it, an excess of mercury is covered with nitric acid (25 per cent) and allowed to stand in a cool place for several days (2). When crystals begin to form, the solution is warmed and separated from the excess of mercury by filtration through an asbestos

pad on a Gooch crucible. A fairly pure salt crystallizes from the filtrate.



Mercurous nitrate is used in the manufacture of yellow mercurous iodide (*q. v.*). Mercurous nitrate is employed to some extent as a laboratory reagent. For microscopic analysis, an aqueous solution of the salt, known as *Millon's reagent*, is prepared by dissolving 3 cc. of mercury in 27 cc. of fuming nitric acid without heat. This is diluted with an equal volume of water. It gives a pink color or brick red precipitate with protein substances, *e. g.*, albumin, urea, etc., and hence is used in their detection.

## BORON, ALUMINUM AND THE METALS OF GROUP III

**Introduction.**—In the next five chapters, boron, aluminum, and the metals of the Earths will be considered. Of the elements that form Group III in Mendeléeff's Periodic Table, boron and aluminum are of the greatest interest and importance to the pharmacist. Besides the two elements just mentioned, the group contains two subgroups of metallic elements which are neither well known nor abundant. The elements of Division A are *gallium* (Ga, atomic weight, 69.72), *indium* (In, atomic weight, 114.76) and *thallium* (Tl, atomic weight, 204.39). Division B contains the elements *scandium* (Sc, atomic weight, 45.1), *yttrium* (Y, atomic weight, 88.92), *lanthanum* (La, atomic weight, 138.92) and a large number of elements having atomic numbers from 59 to 71, inclusive, known as the *rare-earth elements*.

The general properties of the members of this group are as follows: As a rule, they are trivalent and form oxides of the general formula  $R_2O_3$  and chlorides of the general formula  $RCl_3$ . The elements of Division A resemble aluminum by forming *alums* that have a general formula  $U_2SO_4 \cdot T_2(SO_4)_3 \cdot 24H_2O$  in which U is a univalent metal, *e. g.*, potassium, and T is a trivalent metal, *e. g.*, aluminum.<sup>1</sup> Boron, scandium, yttrium, lanthanum, and the rare-earth elements do not form alums. The salts of the elements of both Divisions A and B possess the property of forming molecular compounds with organic substances.

Boron is a non-metal which exhibits a chemical behavior analogous to silicon. Its compounds also resemble those of both silicon and carbon. Its normal valence is 3, although a possible valence of 5 has been assigned to it. Boron trioxide is a feebly acidic oxide. However, it seems to react as a very weak base toward very strong acids.

Aluminum hydroxide is amphoteric and possesses slightly more basic than acidic properties. The metallic hydroxides of the elements in Division A are also amphoteric. The basic character, however, increases as the atomic weight increases.

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### CHAPTER XXV

#### BORON AND BORON COMPOUNDS

##### BORON

Symbol, B. Valence, 3. Atomic Weight, 10.82; Atomic Number 5

**History and Occurrence.**—J. Gay-Lussac and L. Thénard isolated the impure element in 1808 by heating boron trioxide (*q. v.*) with

<sup>1</sup> See also p. 442.

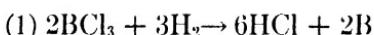
potassium carbonate in an iron retort. Sir Humphrey Davy obtained it about the same time from boric acid.

Boron does not occur free in Nature. In combinations containing oxygen, it is found as boric acid, borax, tincal, boracite, borocalcite, colemanite, etc. (See Boric Acid, Sodium Tetraborate, p. 100.)

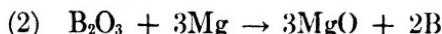
**Physical Properties.**—Pure boron is an amorphous, brown powder having a density of 2.45. It is stable in air. This non-metallic element belongs to the aluminum family (Group III).

**Chemical Properties.**—With a few possible exceptions, boron is trivalent and its oxide and hydroxide are acidic. The chemical behavior of boron resembles that of silicon, and the chemical properties of its compounds bear a close relationship to those of both silicon and carbon. The element sublimes in the electric arc and burns on very strong ignition, producing boron trioxide ( $B_2O_3$ ) and boron nitride (BN). At ordinary temperatures, boron is a poor conductor of electricity but as the temperature rises its electrical conductivity rapidly increases. As previously stated, the chemical behavior of boron closely resembles that of silicon. Concentrated nitric or sulfuric acids oxidize it to boric acid. It burns in oxygen at 700° C. Fluorine combines with it at ordinary temperatures. Chlorine, bromine and sulfur unite with it at 410° C., 700° C., and 600° C., respectively. It does not combine with iodine. When heated to redness with magnesium, it forms a boride. At higher temperatures, the borides of other metals are also formed. It unites with carbon at the temperature of the electric arc to form boron carbide. It does not react with the alkali metals, but forms alkali borates with fused fixed alkalies. It reduces many metallic oxides ( $PbO$ ,  $CuO$ , etc.) and, at red heat, decomposes water, carbon dioxide, sulfur dioxide, and nitric oxide.

**Commercial Manufacture.**—In 1909, Weintraub prepared the first absolutely pure boron by reducing boron trichloride with hydrogen (1).



H. Moissan<sup>1</sup> prepared the element by heating 3 parts of boron trioxide with 1 part of magnesium powder (2). The resulting dark brown powder was then washed with water, hydrochloric acid, hydrofluoric acid and finally calcined with boron trioxide or with borax, the mass being protected during the operation by a layer of powdered charcoal.



Boron may be made by heating a mixture of potassium borofluoride ( $KBF_4$ ) and metallic sodium in a magnesia-lined crucible, through which a stream of hydrogen is being passed.

Boron trioxide may be readily reduced by heating with aluminum (3).



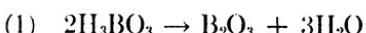
<sup>1</sup> Ann. Chem. Phys., 6, 296 (1895).

## OFFICIAL BORON COMPOUNDS

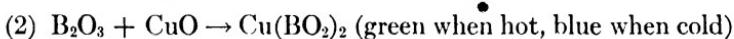
**Boric Acid** ( $H_3BO_3$ ).—(See p. 100.)**Sodium Tetraborate** ( $Na_2B_4O_7$ ).—(See p. 161.)**Sodium Perborate** ( $NaBO_3$ ).—(See p. 205.)

## NON-OFFICIAL BORON COMPOUNDS

**Boric Oxide** (Boron Trioxide) ( $B_2O_3$ .—This oxide of boron is formed by burning amorphous boron in oxygen or by heating boric acid to redness (1).



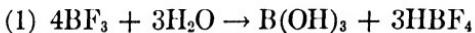
It is a hard, glassy, white solid which only volatilizes at white heat. When boric oxide is heated with various salts, it will displace even the most active acids. When heated with many metallic oxides, it dissolves them and forms fusible, glass-like salts, a number of which are characteristically colored (2).



Boric oxide is used for making glass.

When boric oxide is partially reduced, a so-called suboxide is formed. Because of its deoxidizing properties, it is used like the element to purify molten copper before casting.

**Halogen Compounds of Boron**.—**Boron Fluoride** ( $BF_3$ ).— This colorless fuming gas may be made by the action of hydrofluoric acid on boron trioxide or by the direct union of fluorine with boron. It dissolves very readily in water to form orthoboric acid and fluoboric acid ( $HBF_4$ ) (1). The latter is a very active monobasic acid which forms salts that are only sparingly soluble. Fluoboric acid is also formed by the action of hydrofluoric acid on boron fluoride (2).

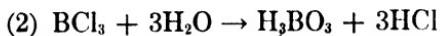


**Boron Bromide** ( $BBr_3$ ).—Boron bromide is a colorless fuming liquid having a boiling-point of  $90^\circ C$ . It has a specific gravity of 2.69 ( $15^\circ C.$ ) and is decomposed by both water and alcohol. It is made by a method analogous to that used for preparing the chloride (*q. v.*).

**Boron Chloride** ( $BCl_3$ ).—This colorless fuming liquid may be obtained by heating boron in a current of chlorine or by passing chlorine over a red-hot mixture of carbon and boric oxide (1).



It boils at  $12.5^\circ C.$ , has a specific gravity of 1.35 ( $15^\circ C.$ ), and is readily decomposed by water (2).



NOTE.—Boron and iodine do not unite.

**Metaboric Acid (HBO<sub>2</sub>).**—(See p. 101.)

**Uses.**—The element boron is never used in medicine or pharmacy. However, in combination as borax, boric acid, sodium perborate, etc., it is extensively employed. These compounds are considered in other chapters. By virtue of the element being a reducing agent, it is used to deoxidize molten copper before it is cast.

## CHAPTER XXVI

### ALUMINUM AND ALUMINUM COMPOUNDS

#### ALUMINUM

Symbol, Al. Valence, III. Atomic Weight, 26.97  
Atomic Number, 13

**History.**—In 1754, Marggraf showed that *alumina* (aluminum oxide,  $\text{Al}_2\text{O}_3$ ) was not identical with lime. In 1825, Hans Christian Oersted obtained the metal by reducing aluminum chloride with sodium amalgam. In 1827, Wöhler reduced the chloride with metallic potassium (1) and obtained the metal.

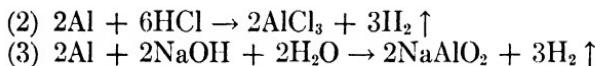


**Occurrence.**—Aluminum *per se* is not found in Nature, although in combination, it constitutes about 7.3 per cent of the earth's crust. In combination, it is found extensively as the oxides, silicates and hydrated oxides. As the oxide, it is native as *corundum* [ $\text{Al}_2\text{O}_3$ ] containing 52.9 per cent of aluminum and as *emery* [ $\text{Al}_2\text{O}_3$ , associated with black oxide of iron]. As the silicate, it is found in rocks, clays [*kaolin*,  $\text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot 2\text{H}_2\text{O}$ , containing 20.9 per cent of aluminum] and shales. (See Talc.) As *cryolite*, a double fluoride,  $\text{Na}_3\text{AlF}_6$ , it occurs notably in Greenland. *Bauxite* [ $\text{Al}_2\text{O}(\text{OH})_4$ ] is a hydrated oxide mixed with ferric oxide. It contains 39.1 per cent of aluminum. It is found in the United States, chiefly in Georgia, Alabama, Tennessee and Arkansas. It is found also in France (see Serpek Process for Nitrogen Fixation) and in British Guiana. Two other hydrated oxides of aluminum, *diaspore* [ $\text{Al}_2\text{O}_3 \cdot \text{H}_2\text{O}$ , containing 45 per cent of aluminum] and *gibbsite* [ $\text{Al}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ , containing 34.6 per cent of aluminum] are commonly present in bauxite ores. Aluminum is always present in the ashes from bird feathers (Gonnermann, 1918). *Spinel* [ $\text{Mg}(\text{AlO}_2)_2$ ] is a naturally occurring mineral and seems to be a salt of metaluminic acid. It is representative of an entire group of minerals collectively called *the spinels*. Other trivalent metals may replace the aluminum, and other bivalent metals may take the place of magnesium to give isomorphous compounds. Some members of the spinels are *gahnite* [ $\text{Zn}(\text{AlO}_2)_2$ ], *chrysoberyl* [ $\text{Be}(\text{AlO}_2)_2$ ], *franklinite* [ $\text{Zn}(\text{FeO}_2)_2$ ], *magnetite* [ $\text{Fe}(\text{FeO}_2)_2$ ], *chromite* [ $\text{Fe}(\text{CrO}_2)_2$ ], etc.

**Physical Properties.**—Aluminum is a silver-white metal, having a specific gravity of 2.7 at 20° C. It is ductile and malleable. When it is heated between 100° C. and 150° C., it can be worked into thin sheets, drawn into wire, punched, stamped, or spun into any desired form. It melts at 658.7° C. and boils at 1800° C. Weight for weight, it is as good a conductor of electricity as copper. Pure aluminum

cannot be worked on a lathe or polished, but when it is alloyed with about 2 per cent of magnesium, it is admirably adapted for such purposes. (See Magnalium.)

**Chemical Properties.** — Aluminum is a very active element. Although tarnishing only slightly in air, aluminum has a great affinity for oxygen and displaces the metals below it in the electro-motive series from their heated oxides. Its stability in air may be explained by the fact that the superficial layer of oxide protects the metal from being further attacked by the oxygen of the atmosphere. Aluminum is not attacked by sulfuric acid, and only slowly by nitric acid. Both dilute and concentrated hydrochloric acid rapidly act upon it (2). Being of an amphoteric character, aluminum readily dissolves in alkali hydroxides with the evolution of hydrogen and the formation of alkali metaluminates (3).



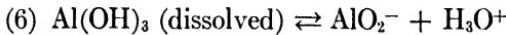
The chemical properties of the aluminum ion are shown in the following reactions: 1. When ammonium hydroxide is added to a solution of an aluminum salt, a gelatinous, white precipitate of aluminum hydroxide is formed (4). The precipitate is insoluble in a moderate excess of the precipitant. When the precipitate is washed and dried at a temperature not exceeding 40° C., it has the approximate composition  $\text{Al}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ .



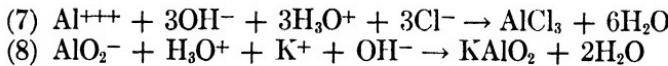
2. When an alkali hydroxide is added to a solution of an aluminum salt, aluminum hydroxide is formed (see equation 4). The precipitated aluminum hydroxide is soluble in an excess of the alkali. Because of its amphoteric character, it is quite evident that dissolved aluminum hydroxide may dissociate in two ways (5 and 6).



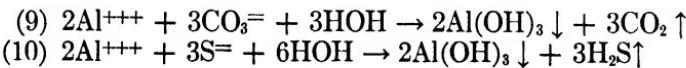
and



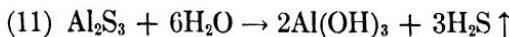
Therefore, salts are formed in the presence of acids (7), and in the presence of strong bases, metaluminates result (8).



3. When alkali carbonates or soluble sulfides are added to a solution of an aluminum salt, aluminum hydroxide (soluble in an excess of either precipitant) is precipitated (9 and 10).



Aluminum carbonate ( $\text{Al}_2(\text{CO}_3)_3$ ) and aluminum sulfide ( $\text{Al}_2\text{S}_3$ ) are completely hydrolyzed by water (11) and, therefore, cannot be made by the action of a soluble carbonate or sulfide upon a solution of an aluminum salt.



4. When a dry aluminum salt is heated on charcoal with a blow-pipe, aluminum oxide is formed. If this is moistened with a solution of cobalt nitrate and again heated, a blue mass of cobalt metaluminite [ $\text{Co}(\text{AlO}_2)_2$ ] is formed (Thénard blue).

5. The Use of Aurin Tricarboxylic Acid (Ammonium Salt) for the Detection of Aluminum.<sup>1</sup>

Dissolve a little freshly prepared aluminum hydroxide in 5 cc. of N-HCl. Add 8 cc. of 2N ammonium acetate and 3 cc. of a 0.5 per cent aqueous solution of the ammonium salt of aurin tricarboxylic acid. On shaking, an insoluble lake will be formed in a few minutes. Add ammonium hydroxide to the solution until it is alkaline, and then 1 cc. of N ammonium carbonate solution. The bright red precipitate will persist.

A quantity of aluminum equal to  $2 \times 10^{-5}$  molecules gives an immediate precipitation or a red solution easily distinguishable from the yellow of the dye in alkaline solution. The delicacy of the test is of the order of  $10^{-6}$  molecules of aluminum.

Silicic acid, salts of Sb, Bi, Pb, Hg (mercuric), Sn (stannic), and Ti give white precipitates. With these salts present, the qualitative test may be made without a separation except when the quantity of aluminum is very small.

Salts of Cd, Co, Ni, Ge, In, Mn, Tl, Th, Zn, Zr, and the rare earths give no precipitates. The chromic ion gives a precipitate that is similar to that obtained with aluminum before the neutralization with ammonium hydroxide. This precipitate, however, disappears on the addition of an excess of ammonium hydroxide and ammonium carbonate.

Ferric salts give a deep violet precipitate in the acetic acid solution, the precipitate being converted to a reddish-brown insoluble lake that is stable under the same conditions as the aluminum lake.

Beryllium gives a lake indistinguishable from that of aluminum. The yellow lake dissolves with difficulty in 2N ammonium carbonate leaving a red-colored solution.

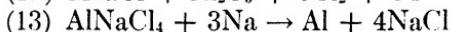
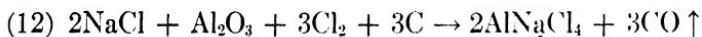
Large amounts of the ions of the alkaline earths give red lakes, but the addition of the carbonate ion converts the alkaline earths to their carbonates and causes the disappearance of the red precipitates.

Phosphates tend to prevent the formation of the aluminum lake, and reducing agents such as hydrogen sulfide and sulfur dioxide destroy the color.

<sup>1</sup> Yoe and Hill: Jour. Am. Chem. Soc., **49**, 2395 (1927). Hammett and Sotterby: Ibid., **47**, 142 (1925).

6. Morin test for aluminum.<sup>1</sup> (This is a very delicate test.) The test solution of aluminum is treated with excess of KOH. A drop of the filtrate is acidified on a black spot plate with 2N acetic acid and a drop of Morin<sup>2</sup> solution added. A green fluorescence appears in the presence of aluminum ion. For very small amounts of Al<sup>+++</sup>, it is desirable to make a comparison with a blank test.

**Commercial Manufacture.**—1. As previously pointed out, Wöhler was the first to produce metallic aluminum by the reduction of its oxide with metallic potassium (1). The cost of the metal prepared by this method was very high (about \$160 a pound) and it was not until 1854, when Deville devised the first working process for the manufacture of aluminum, that the cost dropped to about \$15 a pound. Deville's method consisted in reducing the double chloride of sodium and aluminum with metallic sodium. The former was made by heating together aluminum oxide, charcoal and sodium, and subjecting the mixture to chlorine gas (12). The slag was placed on shallow trays with chips of metallic sodium and heated to redness on the hearth of a reverberatory furnace (13). After several hours, the slag was discarded and the melted aluminum cast into ingot moulds. The Castner process (p. 146) for the manufacture of metallic sodium, greatly reduced the cost of making aluminum by this method.



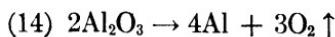
2: Aluminum was first prepared electrolytically by Bunsen in 1854, but, on account of the high melting-point of the chloride, the process was not a commercial success. In 1886, Charles Hall made the metal by the electrolysis of aluminum oxide dissolved in molten cryolite ( $\text{Na}_3\text{AlF}_6$ , melting-point 1000° C.). About the same time, Heroult, a Frenchman, working independently, devised the same method for making metallic aluminum. These methods have been successful commercially and, as a result, the cost of the metal has steadily declined.

The electrolysis is conducted in cells (6 x 3½ feet) lined with carbon, which acts as the cathode. A series of carbon rods serve as the anode and are so arranged that they may be lowered into the fused electrolyte. The cell is partly filled with cryolite and the heat generated by the current is sufficient to melt it. The current is then reduced to between 5 and 6 volts, which is sufficient to maintain the temperature of the melt (875° to 950° C.), and also to cause decomposition. Aluminum oxide (purified bauxite: see Serpek Process, p. 66) is added from time to time. The molten aluminum sinks to the bottom of the cell where it is tapped off, whereas part of the evolved oxygen escapes and part combines with the carbon anodes. The decomposition of purified bauxite ( $\text{Al}_2\text{O}_3$ ) by an electric current

<sup>1</sup> Feigl: Spot Tests, English translation by Matthews, p. 112 (1937).

<sup>2</sup> Solution of a yellow dye ( $\text{C}_{14}\text{H}_{16}\text{O}_7 \cdot 2\text{H}_2\text{O}$ ) from old wood of tropical American tree, *Chlorophora tinctoria*.

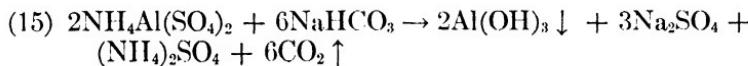
is more than likely accompanied by some complex reactions. Nevertheless, in its simplest form, the decomposition may be represented by equation (14).



**Pharmacological Action of Aluminum Ion.**—Dilute solutions of the soluble salts of aluminum, when applied topically, have the property of constricting the blood vessels. More concentrated solutions precipitate proteins and, therefore, are not only astringent but also antiseptic. The soluble salts of all of the heavy metals are astringent but, in concentrations slightly greater than that required to produce vasoconstriction, they are destructive to tissue and hence irritating and even escharotic. The soluble salts of aluminum, lead and zinc differ from the salts of the other heavy metals by retaining their astringent action over quite a solution—concentration range. Soluble aluminum salts are sometimes taken internally against diarrhea.

Aluminum ion is practically unabsorbed from the alimentary tract and hence large oral doses given over an extended period of time will produce nothing more than local inflammation. The element is excreted in the feces, principally as the phosphate.

The action of diluted acids upon aluminum cooking utensils is so slight as to be negligible. The use of ammonium alum in baking powders for the purpose of liberating carbon dioxide from sodium bicarbonate (15) is considered by some to be a most serious objection to the use of the so-called "alum baking powders." No doubt some of the aluminum hydroxide formed during the reaction is dissolved by the hydrochloric acid and proteins in the stomach. On the other hand, the Referee Board of 1914 was unable to detect any aluminum in the blood after orally administering 1 Gm. of alum per day for four days.



**Uses.** — Because of its lightness, strength and non-corrosive property, aluminum is used in making cooking utensils, instruments, aluminum paints and structural devices of all kinds. In the making of steel castings, about 1 ounce of aluminum is added to 1 ton of molten metal in order that any free oxygen or nitrogen may combine with it as oxide ( $\text{Al}_2\text{O}_3$ ) or nitride ( $\text{AlN}$ ) and thus prevent the castings from being unsound. In this capacity, aluminum is said to act as a "scavenger metal."

Aluminum readily forms alloys with most metals, lead being an exception. Tin containing some aluminum is harder and more elastic than tin itself; zinc-aluminum alloys are used for soldering aluminumware; aluminum-bronze, consisting of 90 to 98 per cent of aluminum and 2 to 10 per cent of magnesium, is very easily worked on a lathe and will also take a high polish.

Aluminum oxide has a very high heat of formation ( $\frac{1}{3} \text{ Al}_2\text{O}_3 =$

127,000 calories). At elevated temperatures, aluminum will reduce almost all metallic oxides. A German chemist, Goldschmidt, utilized this property to obtain the metals from such difficultly reducible oxides as chromium oxide, uranium oxide, manganese oxide, etc., and he called his process "aluminothermy." When a mixture of powdered aluminum, iron, and iron oxide is placed in a large crucible and ignited by a piece of burning magnesium ribbon, a violent reaction occurs with the formation of molten iron (temperature about 3000° C.) and aluminum oxide



The intense heat and molten metal are used to weld together broken pieces of machinery, *e.g.*, rails, fly wheels, propeller shafts, etc., which cannot be conveniently taken to shops. A mixture consisting of 24 per cent of aluminum and 76 per cent of magnetic or black oxide of iron is known as *thermit*. This mixture was used very effectively as an incendiary during World War II. Thermit mixture requires a temperature of about 1800° C. for ignition. This temperature may be obtained by igniting a mixture of powdered aluminum and barium peroxide with black powder, which is started by an ordinary fuse. Thermit mixtures whose ingredients were "bound" together by water glass or sulfur were known as "*calorite*" and "*daisite*," respectively.

F. Chabert<sup>1</sup> claims that fabrics can be waterproofed by impregnating them with a heavy benzine (b. p. 160° C.) solution of aluminum dust, paraffin wax, and a suitable plasticizing agent, *e.g.*, Para rubber.

#### OFFICIAL COMPOUNDS OF ALUMINUM

##### ALUMINUM CHLORIDE

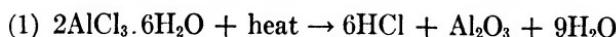
###### *Aluminum Chloride*, N. F. VIII

Formula,  $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$ . Molecular Weight, 241.44

**Physical Properties.**—Aluminum Chloride is a white or yellowish-white crystalline powder. It is odorless and has a sweetish, very astringent taste. It is deliquescent. It has a specific gravity of 2.44 at 25° C.

One Gm. of the salt is soluble in about 0.5 cc. of water and in about 4 cc. of alcohol, at 25° C. It is soluble also in ether and in glycerin.

**Chemical Properties.**—When the hexahydrate is heated, it decomposes into hydrogen chloride and aluminum oxide (1).



The chemical properties of a solution of the salt are due to the aluminum ion (*q. v.*) and the chloride ion (see p. 173).

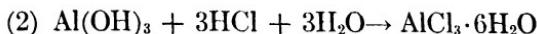
**Official Tests for Identity.**—1. Solutions of aluminum chloride yield with ammonia T.S. a gelatinous white precipitate which is

<sup>1</sup> British Patent, 414, 212.

insoluble in an excess of ammonium hydroxide (see Aluminum Ion Reaction (4), p. 428).

2. Sodium hydroxide T.S. or sodium sulfide T.S. produce the same precipitate which is soluble in an excess of either of these reagents (see Aluminum Ion, *q. v.*).

**Commercial Manufacture.**—1. When aluminum or its hydroxide is treated with hydrochloric acid, aluminum chloride is formed. Upon concentrating the liquid and allowing it to cool, crystals of the hexahydrate separate out (2).



2. Anhydrous aluminum chloride ( $\text{AlCl}_3$ ) may be made by subjecting heated metallic aluminum to a current of dry chlorine (3), or by passing chlorine over a mixture of aluminum and carbon at red heat (4).



The product is a white crystalline solid which melts at  $194^\circ\text{ C}$ . Its vapor density indicates the formula,  $\text{Al}_2\text{Cl}_6$ . However, at  $450^\circ\text{ C}$ .,  $\text{Al}_2\text{Cl}_6$  dissociates into vapors having a density that correspond to the formula,  $\text{AlCl}_3$ .

**Pharmaceutical Preparations and Uses.**—1. *Aluminum Chloride* (Alumini Chloridum), N. F. VIII.—Aluminum Chloride, when dried over sulfuric acid for twenty-four hours, contains not less than 95 per cent of  $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$  (241.44). This salt is sometimes used to check persistent diarrhea. It is employed externally as a general astringent and antiseptic. Solutions of aluminum chloride are used as deodorants (to prevent odor of perspiration). Anhydrous aluminum chloride is used industrially as a catalytic agent and in petroleum refining. It is also used in various organic syntheses (Friedel and Crafts' reaction).

2. *Aluminum Chloride Solution* (Liquor Alumini Chloridi), N. F. VIII.—Aluminum Chloride Solution contains, in each 100 cc., not less than 22.5 Gm. and not more than 27.5 Gm. of  $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$ . Aluminum Chloride is dissolved in water and filtered, if necessary, to obtain a clear product. Externally it is to be used undiluted on the unbroken and non-irritated skin for the astringent and anti-septic action.

## ALUMINUM HYDROXIDE

### *Aluminum Hydroxide Gel*, U. S. P. XIII

Formula,  $\text{Al(OH)}_3$ . Molecular Weight, 77.99

**Physical Properties.**—It is a white, viscous suspension, translucent in thin layers, from which small amounts of water may separate on standing. Aluminum hydroxide is insoluble in water but readily soluble in acids.

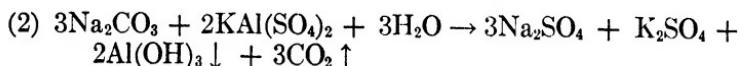
**Chemical Properties.**—Aluminum hydroxide gel is amphoteric in character. It slightly affects both red and blue litmus paper, but does not affect phenolphthalein T.S. When it is heated to redness, it decomposes into water and aluminum oxide. The hydroxide reacts readily with acids, such as hydrochloric acid, forming water and the aluminum salt (1).



This solution responds to all the reactions of the aluminum ion (*q. v.*).

**Official Tests for Identity.**—A hydrochloric acid solution of aluminum hydroxide gel responds to the tests for the *Aluminum ion* (see p. 432).

**Laboratory Preparation and Commercial Manufacture.**—Dissolve 20 Gm. of powdered potassium and aluminum sulfate (potassium alum) and 9 Gm. of monohydrated sodium carbonate, each in 200 cc. of water, filter and heat the solutions to boiling. To the hot solution of sodium carbonate contained in a capacious vessel, gradually and with constant stirring add the hot solution of alum (2) (see p. 442). Add 500 cc. of boiling water and allow the precipitate to subside. Carefully decant the supernatant liquid and again add 500 cc. of *hot* water. When the precipitate has settled, pour off the clear liquid, and wash it with *hot* water until the washings fail to give more than a faint cloudiness with barium chloride test solution.

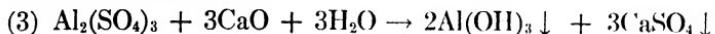


It will be noted that the alum solution is *added to* the solution of sodium carbonate. It has been observed that aluminum hydroxide, prepared by adding the carbonate solution to that of the alum, persistently retains the alkali sulfate and hence is difficult to wash. *Hot* water, not *boiling* water, should be used to wash the precipitate because the latter tends to decompose the aluminum hydroxide.

**Uses.**—It is employed in the dyestuffs industry as a mordant. Freshly precipitated aluminum hydroxide combines with many organic dyes (alizarin and anthracene derivatives, etc.) to form insoluble combinations of different colors which are known as *lakes*. These insoluble, colored compounds are used as pigments. When it is desired to dye a fabric with a *fast* color, the cloth is first soaked in a solution of an aluminum salt, such as the acetate. The cloth is then exposed to steam which completely hydrolyzes the aluminum acetate to acetic acid and aluminum hydroxide. The acetic acid is volatilized by the steam and the aluminum hydroxide remains in the fiber. The cloth is then dipped in a solution of the dye and the color is fixed in the fibers by the formation of these *lakes*. Water-proof fabrics are made by immersing the materials in a solution of aluminum acetate and exposing them to the action of steam and heat. In this way the fibers are first impregnated with

aluminum hydroxide which, when heated, changes to aluminum oxide. The impregnation of the fibers renders them non-porous and therefore they are not wetted by water.

Because of its gelatinous character when freshly precipitated, and because of its mild astringency, aluminum hydroxide is used in water purification. Alum cake (impure aluminum sulfate made by the action of sulfuric acid upon bauxite) is dissolved in the water and the hydroxide precipitated by the addition of lime (3). As the gelatinous precipitate settles out, it carries with it all suspended matter, even microorganisms.



When freshly precipitated aluminum hydroxide is added to a turbid or colored liquid (vegetable juices, etc.) the suspended materials and coloring matter contained therein are precipitated, hence its use as a clarifying and decolorizing agent. A mixture known as *Alumina Cream* is used for this purpose. It is made by dividing a saturated aqueous solution of potassium alum into two *unequal* parts. A slight excess of ammonium hydroxide is added to the *larger* portion, and then small amounts of the *smaller* portion are added to the resulting mixture until the same is slightly acid to litmus. The property possessed by even dilute solutions of aluminum salts, *viz.*, that of precipitating proteins is made use of in the purification of toxins and antitoxins.

**Pharmaceutical Preparations and Uses.**—1. *Aluminum Hydroxide Gel* (Gelatum Alumini Hydroxidi, Colloidal Aluminum Hydroxide), U. S. P. XIII.—Aluminum Hydroxide Gel is a suspension containing the equivalent of not less than 3.6 per cent and not more than 4.4 per cent of  $\text{Al}_2\text{O}_3$ , chiefly in the form of aluminum hydroxide. It is a white viscous suspension, translucent in thin layers, from which small amounts of water may separate on standing.

The Pharmacopœia permits a sufficient amount of oil of peppermint, glycerin, sucrose, or saccharin to be added for flavoring and other purposes. Sodium benzoate or benzoic acid in an amount not to exceed 0.5 per cent may be used as a preservative.

Colloidal Aluminum Hydroxide is used as an antacid and protective in treating peptic ulcers. Because its insolubility precludes excessive alkalinization, and because the aluminum ion formed by its solution in the hydrochloric acid of the stomach makes it astringent and also antiseptic, colloidal aluminum hydroxide has a distinct advantage over soluble alkalies. Intestinal bacteria are also adsorbed by the aluminum hydroxide not dissolved in the stomach. It is used in cases of marked hyperacidity. It decreases the secretion of total and free acid and few ill-effects have been observed as a result of its use. Depending upon the severity of the lesion in cases of peptic ulcer, it may be administered orally in divided doses totalling 1 to 5 fluidounces of the gel daily. It is also administered with great effectiveness against the hyperchlorhydria of ulcer patients by the so-called continuous intragastric drip

method. It acts principally by buffering against the excess acid. A teaspoonful will neutralize over  $1\frac{1}{2}$  fluidounces of  $\frac{N}{10}$  gastric juice.

Average dose—8 cc. (approximately 2 fluidrachms).

2. *Dried Aluminum Hydroxide Gel* (*Gelatum Alumini Hydroxidi Siccum*), U. S. P. XIII.—“Dried Aluminum Hydroxide Gel, when ignited to constant weight, yields not less than 50 per cent of  $\text{Al}_2\text{O}_3$ .” Dried Aluminum Hydroxide Gel is a white, odorless, tasteless, amorphous powder, which is insoluble in water and in alcohol. It is soluble in diluted mineral acids and in solutions of fixed alkalies.

Dried Aluminum Hydroxide Gel may be suspended in distilled water to make the official Aluminum Hydroxide Gel. Dried Aluminum Hydroxide Gel is used externally as a mild astringent and desiccant and internally as an antacid and protective. It is infrequently used in the treatment of diarrhea and cholera, externally as a dusting powder for desiccating foul wounds, etc. It is a constituent of some foot powders. Average dose—0.6 Gm. (approximately 10 grains).

### ALUMINUM PHOSPHATE

*Aluminum Phosphate Gel*, U. S. P. XIII

Formula,  $\text{AlPO}_4$ . Molecular Weight, 121.95

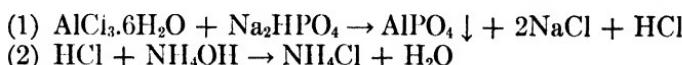
**Physical Properties.**—Aluminum Phosphate Gel is a white, viscous suspension from which small amounts of water may separate on standing. Aluminum phosphate is insoluble in water but readily soluble in acids. The pH of the gel at 25° C. is between 6 and 7.2.

**Chemical Properties.**—Aluminum Phosphate Gel reacts with nitric or hydrochloric acids to form a clear solution. These acid solutions respond to the reactions of the phosphate ion (see p. 207) and the aluminum ion (see p. 428) respectively.

**Official Tests for Identity.**—1. A solution of aluminum phosphate gel in hydrochloric acid responds to the tests for aluminum ion (*q. v.*).

2. A solution of the gel in diluted nitric acid responds to the tests for phosphate ion (see p. 127).

**Commercial Manufacture.**<sup>1</sup>—“Thirty-six (36) pounds of aluminum chloride are dissolved in any suitable vessel in twenty (20) gallons of water. Twenty-one (21) pounds of dried dibasic sodium phosphate are dissolved in twenty-two and one-half (22½) gallons of water and this second solution added slowly to the solution of aluminum chloride in water previously formed. When the reaction (1) of forming the aluminum phosphate is complete the combined solution is neutralized with diluted ammonia water to a pH of between 6.8 to 7.4 (2).



<sup>1</sup> U. S. patent 2,294,889 September 8, 1942.

The mixture is strained and washed until it is practically free from soluble salts when sufficient water is removed so that the mixture shows a strength of 4 per cent of aluminum phosphate. In order to make the product more palatable sweetening agents such as glycerin, sugar, or saccharin may be added and a flavor such as oil of peppermint additionally incorporated, if desired.

The product of the above example in the fluid form having a strength of 4 per cent of aluminum phosphate is the preferred product which has given the best results. A partially or totally dried product, or one containing a higher concentration of aluminum phosphate may be prepared by control of the dehydration step, in order to give convenience of administration or greater strength of aluminum phosphate, as desired."

**Pharmaceutical Preparations and Uses.**—1. *Aluminum Phosphate Gel* (Gelatum Alumini Phosphatis), U. S. P. XIII.—"Aluminum Phosphate Gel is a water suspension containing not less than 3.8 per cent and not more than 4.5 per cent of  $\text{AlPO}_4$ ."

The Pharmacopœia permits a sufficient amount of oil of peppermint, glycerin, sucrose, or saccharin to be added for flavoring and other purposes. Sodium benzoate or benzoic acid may be added in an amount not to exceed 0.5 per cent as a preservative.

Aluminum phosphate gel possesses antacid, astringent and demulcent properties analogous to those of aluminum hydroxide gel, and it provides an effective and safe method of promoting the healing of peptic ulcer,<sup>1</sup> but, unlike aluminum hydroxide gel, it does not interfere with the absorption of phosphates from the intestines. This gel is of particular value for the management of peptic ulcer in the presence of a relative or absolute deficiency of pancreatic juice, diarrhea or a low phosphorus diet.<sup>2</sup>

## ALUMINUM SILICATES

### 1. *Bentonite*, U. S. P. XIII

**Physical Properties.**—Bentonite is a native colloidal, hydrated aluminum silicate. It is a very fine, odorless, tasteless, and practically colorless powder, free from grit. It also occurs as small granules. It is insoluble in water, but swells to about twelve times its volume when added to water, and produces an opalescent suspension or paste. It is insoluble in organic solvents and does not swell in them.

**Chemical Properties.**—An aqueous solution of bentonite is alkaline in reaction and has a pH of 9 to 10. Bentonite is of variable composition but about 90 per cent is *montmorillonite* [ $\text{H}_2\text{O} \cdot (\text{Al}_2\text{O}_3 \cdot \text{Fe}_2\text{O}_3 \cdot 3\text{MgO})4\text{SiO}_2 \cdot n\text{H}_2\text{O}$ ]. It is similar to kaolin chemically but is made up of smaller particles and has a greater adsorptive capacity.

**Official Tests for Identity.**—1. A gel prepared from 6 Gm. of bentonite and 300 mg. of magnesium oxide in 200 cc. of water is

<sup>1</sup> Surg. Clin. North America, 21, 743 (1941).

<sup>2</sup> Arch. Int. Med., 67, 563 (1941).

agitated for one hour. One hundred cc. of the mixture is transferred to a 100 cc. cylinder, and allowed to remain undisturbed for twenty-four hours. Not more than 2 cc. of supernatant liquid should appear on the surface.

2. Swelling power: when 2 Gm. of bentonite is added to 100 cc. of water in a 100 cc. cylinder the mass occupies an apparent volume of not less than 24 cc.

3. Fineness of powder: when an aqueous suspension is passed through a No. 200 standard mesh sieve, no grit is felt when the fingers are rubbed over the wire mesh of the sieve.

4. When dried at 110° C. to constant weight, bentonite loses not less than 5 per cent and not more than 8 per cent of its weight.

**Commercial Manufacture.**—Kaolin is mined as such in different parts of the United States but most of it comes from Wyoming and South Dakota.

**Pharmaceutical Preparations and Uses.**—1. *Bentonite* (Bentonitum), U. S. P. XIII.—Bentonite is a native, colloidal, hydrated aluminum silicate. It is used to stabilize emulsions, as a detergent in cleaners, as a clarifying agent, as an adsorbent for coloring matter, and as a suspending agent.

2. *Bentonite Magma* (Magma Bentoniti), U. S. P. XIII.—This is a preparation containing 5 per cent of bentonite in suspension in distilled water. It is used where the properties of bentonite are desired.

3. *Calamine Lotion* (Lotio Calaminæ), U. S. P. XIII.—Bentonite magna (40 per cent) is used to lessen the rapid sedimentation rate of the calamine and zinc oxide.

## 2. *Kaolin*, N. F. VIII

**Physical Properties.**—Kaolin is a native hydrated aluminum silicate, powdered, and freed from gritty particles by elutriation. It occurs as a soft, white or yellowish-white powder, or as lumps. It has a clay-like or earthy taste and, when moistened with water, assumes a darker color and develops a marked clay-like odor. It is insoluble in water, in cold dilute acids and in solutions of the alkali hydroxides.

**Chemical Properties.**—Kaolin is chemically inert since it is insoluble in all of the common solvents.

When treated with sulfuric acid and strongly heated, aluminum sulfate and silicon dioxide form (see below).

Nearly all igneous rocks contain aluminum silicate ( $\text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot 2\text{H}_2\text{O}$ ) in some combined form, *e. g.*, the double silicates of aluminum and the alkali metals [*feldspar*,  $(\text{SiO}_3)_2\text{AlK} \cdot \text{SiO}_2$ ; *lencite*  $(\text{SiO}_3)_2\text{AlK}$ ; etc.]. Weathering permits the alkali silicates to be removed by rain, leaving large deposits of relatively pure aluminum silicate. When the material is pure and white, it is known as *kaolin* or *kaolinite* and, as indicated, is the principal product of weathering of aluminum minerals such as the feldspars and micas. Aluminum silicate

(principally *kaolinite*,  $H_4Al_2Si_2O_9$ , or a very similar colloid) containing impurities of calcium, magnesium, iron oxides, fragments of quartz, etc., is known as *clay*. A pure, finely divided clay possesses some very definite properties, *viz.*, it takes up water to form a plastic mass that is capable of being moulded (the plasticity probably being due to colloidal materials or "gels" that it contains); a moulded form becomes very hard, retains its shape and contracts from 20 to 40 per cent on burning in suitable furnaces; it loses all of its plasticity upon burning. Because of these inherent properties, clay and kaolin are the principal materials used for the manufacture of bricks, pottery and porcelainware in the ceramic industry.

**Official Tests for Identity.**—1. Mix 1 Gm. of kaolin with 10 cc. of distilled water and 5 cc. of sulfuric acid in a porcelain dish. Evaporate the mixture until the excess of water is removed, and further heat the residue until dense white fumes of sulfuric anhydride appear (1); then cool, add cautiously 20 cc. of distilled water, boil for a few minutes, and filter. A gray residue ( $SiO_2$ ) remains on the filter. The filtrate responds to the tests for *Aluminum* ion (see p. 432).



2. Kaolin loses not more than 15 per cent of its weight upon ignition at red heat.

**Commercial Manufacture.**—Kaolin is present in Nature as clays, the three specific classes being *kaolinite*, *dickite* and *nacrite*. Deposits are found widely distributed over the surface of the earth. Elutriation of the crude clay removes the larger particles of quartz, mica, etc., but in some cases not all of the fine grit. To obtain a colloidal kaolin, the elutriated material may be peptized with sodium pyrophosphate which causes the fine grit to settle out and the fine kaolin particles are retained in suspension. The peptized suspension is then flocculated with another electrolyte and the colloidal kaolin collected.

**Pharmaceutical Preparations and Uses.**—1. *Kaolin* (Kaolinum), N. F. VIII.—"Kaolin is a native hydrated aluminum silicate, powdered and freed from gritty particles by elutriation." Kaolin is used internally for its adsorptive properties. It is useful in diarrhea where the cause is food poisoning or organisms causing dysentery. In cases of intestinal fermentation it helps by adsorbing gases, toxins and bacteria.

Externally it is used as a dusting powder, absorbent in ulcers and moist infections, and in cataplasms as a carrier of heat.

2. *Kaolin Cataplasm* (Cataplasma Kaolini), N. F. VIII.—Kaolin in very fine powder and recently dried at  $110^{\circ}$  C. and boric acid in very fine powder are mixed and made into a mass with warm glycerin. Thymol is dissolved in methyl salicylate and peppermint oil and the solution added to the mass, which is then worked until it is homogeneous. This preparation is used as a mild counter-

irritant and as an antiseptic, cooling dressing. On account of the hygroscopic nature of the glycerin, it must be kept in well-closed containers.

### 3. *Pumice*, N. F. VIII

**Physical Properties.**—Pumice is a substance of volcanic origin, consisting chiefly of complex silicates of aluminum, potassium, and sodium.

Pumice occurs as a gritty, grayish powder or as very light, hard, rough, porous grayish masses. It is tasteless and odorless, and is permanent in air. It is insoluble in all of the usually used solvents. In the large masses, pumice will float on water but due to its porous structure gradually absorbs water and sinks. The specific gravity of pumice is 2.3.

**Chemical Properties.**—Pumice is chemically inert. It is not attacked by acids or alkalies. It is composed of 70 to 75 per cent of silica ( $\text{SiO}_2$ ), 15 to 20 per cent of iron and alum oxides, and traces of calcium, magnesium, potassium and sodium compounds.

**Official Tests for Identity.**—1. Powdered pumice is marketed in three grades each having specific requirements as to fineness.

2. When 10 Gm. of pumice is boiled with 50 cc. of water for thirty minutes and then filtered, the reaction is neutral to litmus paper and one-half of the filtrate yields upon evaporation not more than 10 mg. of residue.

3. When 1 Gm. is boiled with 25 cc. of diluted hydrochloric acid for thirty minutes and filtered, the residue from the filtrate yields not more than 60 mg. of acid-soluble ash.

**Commercial Manufacture.**—Pumice is found in volcanic areas and mined. There are deposits in Italy and the western part of the United States in Nebraska and Oregon.

**Pharmaceutical Preparations and Uses.**—1. *Pumice* (*Pumex*), N. F. VIII.—Pumice is a substance of volcanic origin, consisting chiefly of complex silicates of aluminum, potassium, and sodium. It is used as a distributing agent for slowly soluble substances. Because of its hardness, some use is found for it in dental preparations and cleaners.

## ALUMINUM SULFATE

### *Aluminum Sulfate*, N. F. VIII

Formula,  $\text{Al}_2(\text{SO}_4)_3 \cdot 18\text{H}_2\text{O}$ . Molecular Weight, 666.41

**Physical Properties.**—Aluminum Sulfate occurs in the form of a white crystalline powder, in shining plates, or in crystalline fragments. It is odorless and has a sweetish, astringent taste. It is stable in air, but hydrolyzes in solution.

One Gm. of aluminum sulfate is soluble in about 1 cc. of water at 25° C., and 11.3 Gm. are soluble in about 1 cc. of boiling water. It is insoluble in alcohol.

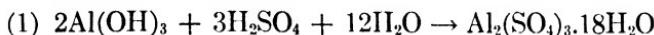
When the salt is gradually heated to about 200° C., it loses

its water of hydration (about 48.6 per cent) and at 770° C., it decomposes.

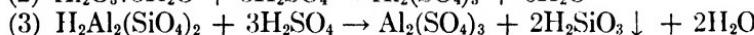
**Chemical Properties.**—An aqueous solution is acid to litmus paper. Aluminum sulfate in solution has the chemical properties of the aluminum ion (see p. 428) and the sulfate ion (see p. 212).

**Official Tests for Identity.**—The salt in solution (1 to 10) responds to the tests for aluminum (see p. 432) and for sulfate (see p. 212).

**Commercial Manufacture.**—1. A very pure grade of aluminum sulfate can be made by dissolving aluminum hydroxide in sulfuric acid (1). When the solution is concentrated and allowed to crystallize, aluminum sulfate with 18 molecules of water of hydration,  $\text{Al}_2(\text{SO}_4)_3 \cdot 18\text{H}_2\text{O}$ , separates out.



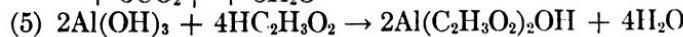
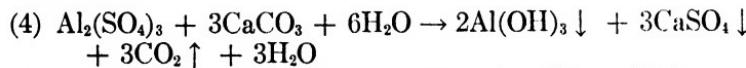
2. Aluminum sulfate for industrial uses is made either by the action of sulfuric acid on bauxite (2), or by digesting clay (impure aluminum silicate) or kaolin (pure, white aluminum silicate) in sulfuric acid (3).



In the latter case, the silicic acid is removed by filtration and the filtrate evaporated to crystallization. During the solidification, the liquid is stirred continuously with wooden paddles to keep the salt from "caking."

**Pharmaceutical Preparations and Uses.**—1. *Aluminum Sulfate* (Alumini Sulfas), N. F. VIII.—Aluminum Sulfate contains not less than 99.5 per cent of  $\text{Al}_2(\text{SO}_4)_3 \cdot 18\text{H}_2\text{O}$ . It is never used internally in pharmacy. Solutions of the salt are antiseptic and astringent. Its principal use is in the preparation of alum and aluminum subacetate solution.

2. *Aluminum Subacetate Solution* (Liquor Alumini Subacetatis), N. F. VIII.—This solution should yield, from each 100 cc., not less than 2.3 Gm. and not more than 2.6 Gm. of  $\text{Al}_2\text{O}_3$ , and not less than 5.43 Gm. and not more than 6.13 Gm. of  $\text{CH}_3\text{COOH}$ . Precipitated calcium carbonate is gradually added to an aqueous solution of aluminum sulfate (4). Acetic acid is then added, and the mixture set aside for several days (5). The clear liquid is syphoned off and after the magma has been pressed, sufficient water is poured through it to make the required volume. This preparation is used in much the same manner as the aluminum acetate solution.



Because of the low cost of manufacture and because of its property of hydrolyzing readily in solution, it affords an excellent source of aluminum hydroxide. The industrial uses of the latter (dyeing,

water purification, etc.) have already been discussed under Aluminum Hydroxide (*q. v.*).

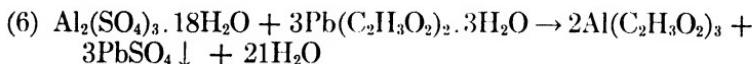
*3. Aluminum Acetate Solution* (Liquor Alumini Acetatis, Burow's Solution), N. F. VIII.—This solution should yield, from each 100 cc., not less than 1.2 Gm. and not more than 1.45 Gm. of  $\text{Al}_2\text{O}_3$ , and not less than 4.24 Gm. and not more than 5.11 Gm. of  $\text{CH}_3\text{COOH}$ , corresponding to not less than 4.8 Gm. and not more than 5.8 Gm. of  $\text{Al}(\text{C}_2\text{H}_3\text{O}_2)_3$  in each 100 cc.

This solution may be prepared by adding glacial acetic acid (15 cc.) to aluminum subacetate solution (545 cc.). The solutions are well mixed and filtered if necessary. The finished solution should have a specific gravity of about 1.022 at 25° C., and should be dispensed only when clear.

Regardless of what method is used in its preparation, this solution must meet the N. F. VIII requirements for strength, quality, and purity. It is permissible to stabilize the preparation by adding not more than 0.6 per cent of boric acid.

In the average dilution with 9 volumes of water, this preparation is used on the skin as a mild astringent and antiseptic. The 5 per cent solution is said by some to possess definite germicidal properties, and a 1 per cent dilution is considered a good antiseptic.<sup>1</sup>

The N. F. VII gives a method of preparing the solution that has the disadvantage of requiring more time, and results in having lead as an impurity (exceeding heavy metals limit of 10 parts per million). Aluminum sulfate and lead acetate are dissolved separately in water. The solution of the latter is poured in a thin stream into the constantly agitated solution of the former (6). The mixture is then set aside in a cold place (about 10° C.) for twenty-four hours. The clear supernatant liquid is syphoned off, or, if necessary, the magma is transferred to a filter and sufficient water is added through the magma to make the required volume.



A recent use of Burow's Solution (lead-free) is in the treatment of arthritis. Aluminum acetate solution (2½ fluidounces), syrup cherry (1½ fluidounces) and honey (4 fluidounces) are mixed. Good results have been reported.

### ALUM

#### *Alum*, U. S. P. XIII

Formula,  $\text{AlNH}_4(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ . Molecular Weight, 453.32;  $\text{AlK}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ . Molecular Weight, 474.38

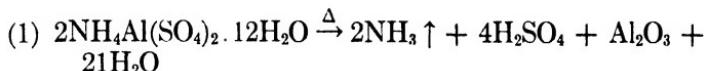
**Physical Properties.**—Alum occurs in the form of large, colorless, octahedral crystals, in crystalline fragments, or as a white powder. It is odorless and has a sweetish, strongly astringent taste.

One Gm. of ammonium alum dissolves in 7 cc. of water at 25° C. and in 0.3 cc. of boiling water. One Gm. of potassium alum dis-

<sup>1</sup> J. Am. Pharm. Assn., Pr. Ed., 3, 132 (1942).

solves in 7.5 cc. of water at 25° C., and in 0.3 cc. of boiling water. Both the ammonium and the potassium alum are freely but slowly soluble in glycerin, but insoluble in alcohol.

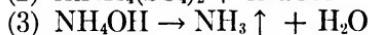
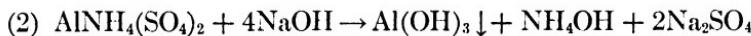
When potassium alum is heated, it melts at 92° C., and loses all of its water at 200° C., forming *burnt alum*. Ammonium alum melts at 95° C., and besides water loses some ammonia and sulfuric acid upon ignition (1).



**Chemical Properties.**—Solutions of alum are acid to litmus paper. The alums are not complex compounds, since the ions of the component salts are formed in solution. Solutions of either alum give the chemical reactions for the aluminum ion (*q. v.*), and for ammonium (see p. 263) or potassium ion (see p. 223).

An alum is a double salt of a trivalent and a univalent element containing 12 molecules of water of hydration. All alums form isomorphous crystals. The trivalent element may be aluminum, iron, chromium, manganese, cobalt, indium, gallium, vanadium, etc., whereas, the univalent radical may be any one of the alkali metals, ammonium, silver or thallous thallium. The most common alums are double sulfates, although double selenates (with the radical,  $\text{SeO}_4^-$ ) are also considered as alums. Potassium or ammonium-aluminum sulfates are the two best known alums. Not infrequently their composition is expressed by the formulas,  $\text{K}_2\text{SO}_4 \cdot \text{Al}_2(\text{SO}_4)_3 \cdot 24\text{H}_2\text{O}$  and  $(\text{NH}_4)_2\text{SO}_4 \cdot \text{Al}_2(\text{SO}_4)_3 \cdot 24\text{H}_2\text{O}$ , respectively.

**Official Tests for Identity.**—1. Sodium hydroxide T.S. added to a solution of ammonium alum (1 in 20) at first produces a precipitate which completely dissolves in an excess of the reagent, ammonia being evolved (2, 3 and 4).



2. Potassium alum undergoes similar reactions to (2) and (4).

3. An aqueous solution of potassium alum responds to all tests for aluminum ion (p. 432), potassium ion (p. 224) and sulfate ion (p. 212).

4. An aqueous solution of ammonium alum responds to all tests for aluminum ion (p. 432), ammonium ion (p. 264) and sulfate ion (p. 212).

**Commercial Methods of Manufacture.**—The various methods now used to make alum are dependent upon the aluminum-containing materials employed. A cursory description of each process is given below:

1. *Alum stone* (alumite) is an abundant mineral occurring in large quantities in Italy. It is a basic alum having the approximate composition  $\text{KAl}(\text{SO}_4)_2 \cdot \text{Al}(\text{OH})_3$ . First, the alum stone is roasted

at 500° C. to render the aluminum hydroxide insoluble and then it is extracted with hot water. When the liquid is concentrated and cooled, large pure cubes of the so-called "*Roman Alum*" crystallize out.

2. Both *bauxite* ( $\text{Al}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ ) and *cryolite* ( $\text{Na}_3\text{AlF}_6$ ) are used in making alum. When either one of these minerals is fused with sodium carbonate, soluble sodium metaluminate is formed. When carbon dioxide is passed into a solution of the latter, aluminum hydroxide is precipitated. The hydroxide is converted into aluminum sulfate by the action of sulfuric acid and the solution is mixed with either potassium sulfate or ammonium sulfate to form the respective alum. Crystals of the alum are obtained by concentrating and cooling.

Alum may be made also by adding a solution of potassium sulfate or ammonium sulfate to a solution of "alum cake" (*q. v.*), and then concentrating the solution to crystallization.

**Pharmaceutical Preparations and Uses.**—1. *Alum* (Alumen), U. S. P. XIII.—Alum contains not less than 99.5 per cent of  $\text{AlNH}_4(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$  or  $\text{AlK}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ . The label of the container must indicate whether the salt is Ammonium Alum or Potassium Alum. Alum precipitates proteins and may, therefore, cause irritant or caustic effects. It is used externally for its astringent properties. Infrequently, alum is orally administered in doses of about 5 grains to remedy a diarrheal condition. One to 5 per cent solutions are used as gargles (somewhat injurious to the teeth) and 0.5 to 1 per cent solutions are employed as urethral injections or as skin lotions.

The protein-precipitation property is used in preparing alum precipitated diphtheria toxoid, alum precipitated diphtheria and tetanus toxoids, and alum precipitated tetanus toxoid.

2. *Exsiccated Alum* (Alumen Exsiccatum, Dried Alum, Burnt Alum), U. S. P. XIII, when recently dried to constant weight at 200° C., contains not less than 96.5 per cent of  $\text{AlNH}_4(\text{SO}_4)_2$  or of  $\text{AlK}(\text{SO}_4)_2$ . It is a white, odorless powder having a sweetish, astringent taste. It absorbs moisture upon exposure to air. One Gm. is very slowly and usually incompletely soluble in about 20 cc. of water at 25° C. It is soluble in about 2 cc. of boiling water. It is insoluble in alcohol. As in the case of Alum, the label of the container must indicate whether it is a nearly anhydrous ammonium alum or potassium alum. It is used as a mild caustic.

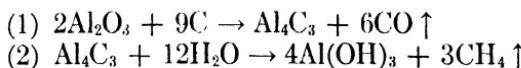
Industrially, alum is sometimes substituted for aluminum sulfate for purposes mentioned in the discussion of the latter.

Alum is also used in the textile and paper industries, for hardening plaster of Paris and in the so-called "alum baking powders." (See p. 431.)

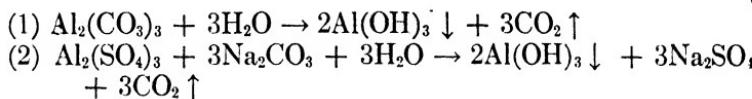
3. *Cochineal Solution* (Liquor Coccii, Cochineal Color), N. F. VIII.—Alum is used in this preparation to form an aluminum lake suitable for coloring alkaline solutions (see p. 232).

## NON-OFFICIAL ALUMINUM COMPOUNDS

**Aluminum Carbide** ( $\text{Al}_4\text{C}_3$ ).—Aluminum carbide is a greenish-gray substance having a density of 2.36. It is made by Moissan's process, which consists in heating aluminum oxide and coke in an electric furnace (1). The product readily reacts with water, yielding methane (2) for which purpose it is used industrially. It is usually shipped in iron drums. It is of little interest to pharmacists.

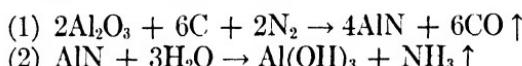


**Aluminum Carbonate** ( $\text{Al}_2(\text{CO}_3)_3$ ).—Aluminum carbonate is completely hydrolyzed by water at the moment of its formation (1). Therefore, when a soluble carbonate is added to a solution of an aluminum salt, the *hydroxide* and *not* the *carbonate* is precipitated (2).



**Aluminum Citrate.**<sup>1</sup>—This salt is commercially available as a glassy crystalline substance which may be readily ground to a fine powder. It is slowly soluble in cold water but very soluble in boiling water. Solutions of the salt are useful as a replacement for aluminum acetate solution.<sup>2</sup> It is fully as effective as Burow's Solution, is more constant in its action and, although not tolerated in every case, complaints of irritation are much less frequent. A 6 per cent solution has been found equivalent to the aluminum acetate in Burow's Solution.

**Aluminum Nitride** ( $\text{AlN}$ ).—Aluminum nitride, in the form of small, yellow, rhombic crystals, is formed when a mixture of bauxite and carbon is heated to  $740^\circ \text{ C}$ . in a current of nitrogen (1). In the presence of hot dilute alkalies, or when subjected to steam under pressure, aluminum nitride decomposes into aluminum hydroxide and ammonia (2). (See Serpek Process for the Fixation of Atmospheric Nitrogen, p. 66.)

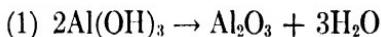


**Aluminum Oxide** ( $\text{Al}_2\text{O}_3$ , alumina).—Aluminum oxide occurs in Nature as corundum, emery, ruby, sapphire, etc. The last two are transparent crystals of aluminum oxide slightly colored by traces of other substances. Aluminum hydroxide, upon ignition, yields a white amorphous powder of aluminum oxide (1), which melts at about  $2050^\circ \text{ C}$ . When the melt is allowed to cool, it resembles natural corundum and is used for making laboratory apparatus. These products are called *alundum ware*. Artificial

<sup>1</sup> Mallinckrodt Chemical Works, St. Louis, Mo.

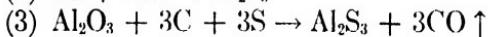
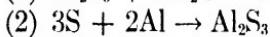
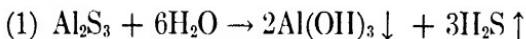
<sup>2</sup> J. Am. Pharm. Assn., Pr. Ed., 3, 132 (1942).

gems may be made by adding small amounts of different metallic oxides to molten alumina. Thus, artificial rubies (red) are made by adding a little potassium bichromate to the melt; artificial amethysts (blue or purple) by the addition of a little cobalt oxide, etc. These artificial gems are identical in properties with the natural stones. These gems are insoluble in acids and therefore must be fused with potassium carbonate before solution can be effected.



Aluminum oxide, combined with silicon dioxide ( $\text{Al}_2\text{O}_3 \cdot \text{SiO}_2$ ) is found in apparently inexhaustible quantities in the Inyo Mountains in California. It is known as *cyanite*, *sillimanite*, and *andalusite*. Because of its strength and resistance to changes in temperature, it is admirably suited for making spark plug bodies and chemical laboratory ware.

**Aluminum Sulfide** ( $\text{Al}_2\text{S}_3$ ).—Aluminum sulfide, as has been pointed out previously, cannot be made by the action of a soluble sulfide on a solution of an aluminum salt, because it is completely hydrolyzed by water (1). However, it may be prepared as yellowish-gray lumps (m. p. 1100° C.) by heating a mixture of aluminum and sulfur to a high temperature (2) or by passing sulfur vapor over a heated mixture of carbon and alumina (3). Moist air decomposes it to a gray powder, and for this reason it is used as a source of  $\text{H}_2\text{S}$  gas.



**Fuller's Earth.**—It is a clay-like material, having a high water content and, like clay, is produced by the weathering of aluminum-bearing minerals. It differs from clay in that it has a very low plasticity. Fuller's Earth is related to kaolin and possesses practically the same properties. It has absorbing and water-binding properties, being used as a clarifying agent, filler and absorbent.

## CHAPTER XXVII

### SCANDIUM AND YTTRIUM AND THEIR COMPOUNDS

#### SCANDIUM

Symbol, Sc. Valence, III. Atomic Weight, 45.10;  
Atomic Number, 21

**History and Occurrence.**—Many of the properties of scandium were predicted by Mendeléeff. He chose to call this undiscovered element “*eka-boron*.” About ten years later (1879) the element was discovered by Nilson in the mineral *euxenite*. Its name is derived from Scandinavia, the place where it was first obtained and the native country of its discoverer.

Scandium is widely distributed in Nature, but in very small amounts. Its richest minerals, *wiikite* and *anorthite*, are found in Finland. It has a density of 2.5, melts at 1200° C., and boils at 2400° C.

**Compounds.**—The metal has not been obtained in the free state. Its hydroxide,  $\text{Sc(OH)}_3$ , is less basic than the corresponding compounds of the family, including the rare earths. Scandium oxide ( $\text{Sc}_2\text{O}_3$ ) is more basic than aluminum oxide, as is evidenced by the fact that the carbonate [ $\text{Sc}_2(\text{CO}_3)_3$ ] exists. Scandium chloride has the formula  $\text{ScCl}_3 \cdot 12\text{H}_2\text{O}$ . Like boron it yields both the simple and complex fluorides, such as  $\text{ScF}_3$  and  $\text{Na}_3\text{ScF}_6$ . The nitrate,  $\text{Sc}(\text{NO}_3)_3 \cdot 4\text{H}_2\text{O}$ , and the sulfate,  $\text{Sc}_2(\text{SO}_4)_3$ , are known. The double sulfate,  $\text{Sc}_2(\text{SO}_4)_3 \cdot 3\text{K}_2\text{SO}_4$ , is not an alum.

#### YTTRIUM

Symbol, Y. Valence, III. Atomic Weight, 88.92;  
Atomic Number, 39

**History and Occurrence.**—Yttrium was the first of the elements of this family, rare earths included, to be discovered. The oxide was obtained by Gadolin in 1794 from *gadolinite*, a mineral occurring near Ytterby, a town in Sweden. Cleve obtained the metal as a dark gray powder of metallic luster by the electrolysis of the double chloride of sodium and yttrium. Gadolinite contains, in addition to yttrium, other members of the yttrium family.

**Physical Properties.**—Yttrium melts at 1475° C. and has a density of 4.57.

**Chemical Properties.**—It is slowly converted into the oxide ( $\text{Y}_2\text{O}_3$ ) by cold water, but more rapidly by hot water. Its oxide is the most basic of the yttrium family which consists of dysprosium, holmium, erbium, thulium, ytterbium, lutecium, and yttrium. It is a weaker base than lanthanum oxide. The hydroxide  $\text{Y}(\text{OH})_3$

will absorb carbon dioxide to form the carbonate. It will also liberate ammonia from ammonium salts. The salts of yttrium are colorless.

**Compounds.**—Yttrium salts, when treated with hydrofluoric acid, yield the fluoride,  $2\text{YF}_3 \cdot \text{H}_2\text{O}$ . The chloride is obtained by passing chlorine over a heated mixture of the oxide and carbonate. It forms the hydrate  $\text{YCl}_3 \cdot \text{H}_2\text{O}$ . Yttrium nitrate,  $\text{Y}(\text{NO}_3)_3 \cdot 2\text{H}_2\text{O}$ , is freely soluble in water. Some of the other salts are the phosphate  $\text{YPO}_4 \cdot 2\text{H}_2\text{O}$ , the sulfide  $\text{Y}_2\text{S}_3$ , the carbonate  $\text{Y}_2(\text{CO}_3)_3 \cdot 3\text{H}_2\text{O}$  and the carbide  $\text{YC}_2$ .

## CHAPTER XXVIII

### GALLIUM, INDIUM AND THALLIUM AND THEIR COMPOUNDS

#### GALLIUM

Symbol, Ga. Valence, III. Atomic Weight, 69.72;  
Atomic Number, 31

**History.**—In 1869, Mendeléeff predicted the existence of an element having an atomic number of 31. He called this undiscovered element “*eka-aluminum*” and described its properties with remarkable accuracy. In 1875, Lecoq de Boisbaudran discovered the spectroscopic lines of the element in a sample of zinc blende (*sphalerite*) and named it *gallium* after his native country, France (Gallia).

**Occurrence.**—Gallium is a rare element and is found in small amounts in most samples of zinc blende (*sphalerite*).

**Physical Properties.**—Gallium is a white, lustrous and tough metal, that may be cut with a knife. It melts at 30.8° C. and, because it remains super-cooled, is often considered to be a liquid element like bromine and mercury. It has a density of 5.91.

**Chemical Properties.**—It does not react with water and only slightly with nitric acid. It dissolves in hydrochloric acid and in alkalies. With aluminum, it forms liquid alloys which readily decompose water.

**Commercial Manufacture.**—This metal has been obtained by the electrolysis of an ammoniacal solution of its sulfate.

**Compounds.**—Gallium oxide [ $\text{Ga}_2\text{O}_3$ ], gallium hydroxide [ $\text{Ga}(\text{OH})_3$ ], gallium chloride [ $\text{GaCl}_3$ ], and gallium sulfate [ $\text{Ga}_2(\text{SO}_4)_3$ ] have been prepared and have similar physical and chemical properties to the corresponding aluminum compounds. Gallium forms a true alum,  $\text{Ga}(\text{NH}_4)(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ . The gallium salts are all hydrolyzed by water, and gallium hydroxide, like the hydroxide of aluminum, is amphoteric.

**Uses.**—Gallium has never been used in medicine or in the industries, it being purely of scientific interest.

#### INDIUM

Symbol, In. Valence, I, II, III. Atomic Weight, 114.76;  
Atomic Number, 49

**History.**—In 1863, Reich and Richter discovered this element when they observed its spectroscopic lines in the spectrum of zinc blendes obtained from Freiberg. They named it *indium* from the two remarkably characteristic and brilliant indigo-blue lines of its spectrum.

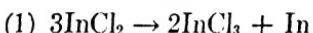
**Occurrence.**—Indium is found in small quantities in zinc blende, and in tungsten, tin, and iron ores.

**Properties.**—Indium is a grayish-white metal that is softer than lead. It has a density of about 7.3 and fuses at 155° C.

It is permanent in air. When heated, it burns with a dark blue flame to form the oxide,  $In_2O_3$ . The metal is more readily attacked by nitric acid than by either hydrochloric or sulfuric acids.

**Commercial Manufacture.**—The metal is made by the reduction of the oxide.

**Compounds.**—The oxides ( $InO$ ,  $In_2O_3$ ,  $In_3O_4$ ) and hydroxide [ $In(OH)_3$ ] of indium resemble the analogous compounds of aluminum. Although amphoteric, their basic character is much more pronounced than that of either aluminum oxide or hydroxide. Indium hydroxide is nearly insoluble in excess of alkali hydroxide. Indium chloride ( $InCl_3$ ) is not hydrolyzed by hot water. However, water acts upon both indium monochloride ( $InCl$ ) and indium dichloride ( $InCl_2$ ) to form indium trichloride ( $InCl_3$ ) and free indium (1).



Indium sulfate forms a true alum with ammonium sulfate.

**Uses.**—Like gallium, indium is never used in medicine.

### **THALLIUM**

Symbol, Tl. Valence, I, III. Atomic Weight, 204.39; Atomic Number, 81

**History.**—Thallium was discovered in 1861 by Crookes, who observed its brilliant green line in the spectrum obtained in the spectroscopic analysis of flue dust secured from a sulfuric acid plant in the Harz Mountains. He named the element *thallium* from the Greek *thallos*, meaning a “green twig.” While investigating the sludges of lead chambers, Lany, working independently, discovered the same element one year later.

**Occurrence.**—Thallium is rather widely distributed in Nature and is more abundant than either gallium or indium. The principal thallium-bearing minerals are Swedish *crooksite*  $[(CuTlAg)_2S$ ; about 17 per cent Tl], *lorandite*  $[TlAs_2S_2$ ; about 60 per cent Tl], and *vrbaita*  $[TlAs_2Sb_6$ ; about 30 per cent Tl]. Small amounts of the elements are found in pyrites, zinc blende, hematite, and traces are found in sylvine and carnallite at Stassfurt and in some mineral springs.

**Physical Properties.**—Thallium is a leaden-colored metal with a hardness about equal to that of sodium. It has a density of 11.2 and fuses at 1845° C. Its vapor density indicates the formula,  $Tl_2$ .

**Chemical Properties.**—The metal is oxidized in moist air, but is permanent when kept under water. It burns with a green flame. It is attacked by nitric acid and by sulfuric acid. It is only slightly soluble in hydrochloric acid, because it soon becomes covered with thallous chloride ( $TlCl$ ) which is difficultly soluble.

**Commercial Manufacture.**—The metal is obtained by dissolving the aforementioned flue dust or sludge in sulfuric acid and precipitating the metal as thallous iodide with hydriodic acid. When the iodide is heated with sodium, sodium iodide (soluble) and metallic thallium (insoluble) result.

**Compounds.**—Thallium forms two series of compounds, *viz.*, thallous compounds, in which the metal is univalent, and thallic compounds, in which the element is trivalent.

Thallous compounds have properties that are similar to those of analogous compounds of silver and of potassium. Thus, the *halides*, *cyanides* and *sulfides* of thallous thallium are insoluble and, in this respect, are like the corresponding compounds of silver. Thallous *sulfate* and *carbonate*, like the corresponding salts of potassium with which they are isomorphous, are soluble in water; the former also yields true alums, whereas, the latter is readily hydrolyzed, giving an alkaline reaction to its solution. Thallous *hydroxide* ( $\text{TlOH}$ ) is a highly ionized base like potassium hydroxide, and a black *thallic oxide* ( $\text{Ti}_2\text{O}$ ) may be obtained by heating it in the absence of air.

Compounds of the *thallic* series markedly resemble the compounds of aluminum and also show some properties that are like the auric compounds. Thus, *thallic hydroxide* [ $\text{Ti}(\text{OH})_3$ ] is a stronger base than aluminum hydroxide. Thallic oxide [ $\text{Ti}_2\text{O}_3$ ], like aluminum oxide, is formed when the hydroxide is heated. *Thallic chloride* [ $\text{TiCl}_3$ ] and *thallic sulfate* [ $\text{Ti}_2(\text{SO}_4)_3$ ] are highly ionizable salts and thus possess properties that lie between those of similar aluminum and auric compounds. Thallic sulfate forms a double sulfate with potassium sulfate [ $\text{K}_2\text{SO}_4 \cdot \text{Ti}_2(\text{SO}_4)_3 \cdot 8\text{H}_2\text{O}$ ] but, on account of its having only 8 molecules of water of hydration, it is not a true alum. Like trivalent gold, thallium forms definite and stable complex ions.

**Uses.**—Thallium acetate has been used in creams as a depilatory. However, it has very toxic effects and may be absorbed through the skin and exert a systemic action. In such cases or when taken orally it causes the loss of body hair. Thallium is very toxic and its use in medicine is unnecessary.

In 1924, the value of thallium salts in the control of various rodents was suggested.<sup>1</sup> In the manufacture of refractive optical glass, it is sometimes used in place of lead.

<sup>1</sup> Munch, J. C., and Silver, J.: Technical Bulletin No. 238, U. S. Dept. of Agriculture (April, 1931).

## CHAPTER XXIX.

### THE RARE-EARTH METALS

It is customary to designate the oxides of the metals having atomic numbers from 59 to 71, inclusive, as the *rare earths*. With the exception of cerium, all the metals belong to Group III of the periodic system. Cerium is tetravalent and has properties which warrant its being placed in Group IV. These elements are divided into three families:

#### I. CERIUM FAMILY

Element	Symbol	Atomic No.	Atomic weight
Lanthanum . . . . .	La	57	138 92
Cerium . . . . .	Ce	58	140 13
Praseodymium . . . . .	Pr	59	140 92
Neodymium . . . . .	Nd	60	144 27
Illinium . . . . .	Il	61	
Samarium . . . . .	Sa	62	150 43

The colors of solutions of the salts of elements 59, 60, 62 and 63 are green, red, pink and rose, respectively, when the metals are trivalent. Salts of the others of like valence yield colorless solutions. Illinium was so recently discovered, that its properties are but little known. These elements yield insoluble double sulfates.

#### II. TERBIUM FAMILY

Element	Symbol	Atomic No.	Atomic weight
Europium . . . . .	Eu	63	152 0
Gadolinium . . . . .	Gd	64	156 9
Terbium . . . . .	Tb	65	159 2

Solutions containing the trivalent Europium ion are pink, whereas those of the other two members of the family are colorless. The double sulfates of all three are moderately soluble.

#### III. YTTRIUM FAMILY (YTTRIUM INCLUDED)

Element	Symbol	Atomic No.	Atomic weight
Yttrium . . . . .	Y	39	88 92
Dysprosium . . . . .	Dy	66	162 46
Holmium . . . . .	Ho	67	164 94
Erbium . . . . .	Er	68	167 20
Thulium . . . . .	Tm	69	169 40
Ytterbium . . . . .	Yb	70	173 04
Lutecium . . . . .	Lu	71	174 99

Trivalent ions of dysprosium and holmium are yellow; those of erbium and thulium are red and green, respectively; the rest are colorless.

**Occurrence.**—Rare-earth metals occur in but few localities. Minerals containing them are found in this country in the Carolinas, and elsewhere in Brazil, Scandinavia, Siberia, Greenland and Africa. Gadolinite contains yttrium and other members of the family. Monazite, an orthophosphate mineral found in Africa, Brazil and the Carolinas, contains the several elements of the cerium family and also such minerals as *zirconia* ( $ZrO_2$ ), *thorite* ( $ThSiO_4$ ), *rutile*

( $\text{TeO}_2$ ), *cassiterite* ( $\text{SnO}_2$ ), *quartz* ( $\text{SiO}_2$ ) and *magnetite* ( $\text{Fe}_3\text{O}_4$ ). The monasite sands produce compounds of thorium and cerium. Both of these metals are used in the production of incandescent gas mantles.

**Valence.**—All the elements of the group act as trivalent metals to form salts. Cerium, as stated, has the valence of 4. Both  $\text{SaCl}_2$  and  $\text{EuCl}_2$  are known. Some of the elements have higher oxides than those of the general formula  $\text{El}_2\text{O}_3$ . Three is therefore the important valence of the group. With this valence they form chlorides, nitrates, sulfates, etc.

**Properties.**—Only the metals of the cerium family have been prepared in a state of purity. They are obtained by reduction. Mixed metal, prepared by the electrolytic reduction of the mixed chlorides of the cerium metals, is used in the reduction of the oxides of various metals. The rare-earth metals unite vigorously with oxygen. They combine also with hydrogen and nitrogen.

**Separation of the Rare Earths.**—Because of their likeness in chemical behavior, the rare-earth metals cannot be separated by the usual methods. This is especially true of the metals of the same family. Hence, special processes are resorted to, among which are the following:

- (a) Fractional decomposition of the nitrates by ignition.
- (b) Fractional crystallization of salts.
- (c) Fractional precipitation of various salts.
- (d) Fractional precipitation by bases of different strengths.

#### INTRODUCTION TO THE ELEMENTS OF GROUP IV

Carbon and silicon belong in the second and third so-called "short periods" of Mendeléeff's Periodic Table of Elements. Both of these elements are characteristically non-metallic in chemical behavior and, like all other members of this group, have a maximum valence of 4. Carbon, but not silicon, exhibits a valence of 2. This bivalence is also characteristic of the other members of this family.

The members of Division A are *germanium*, *tin* and *lead*. These elements are distinctly metallic, although in some instances they show non-metallic properties ( $\text{Na}_2\text{SnO}_3$ , sodium stannate;  $\text{Na}_2\text{PbO}_2$ , sodium plumbite; etc.). As the atomic weights of these elements increase, the more pronounced become the metallic properties. The compounds of these elements have properties that are very similar to analogous compounds of silicon, whereas, toward carbon compounds, the relationship is more distant.

*Titanium*, *zirconium*, *cerium*, *hafnium*, and *thorium* comprise Division B of this group. Titanium closely resembles silicon, but, as the atomic weights of the other elements increase, their similarity to silicon diminishes until in thorium (a definite metallic element), it has entirely disappeared. The properties of all of the elements of this division so closely resemble those of the rare-earth metals that occasionally a few of these elements (*e. g.*, cerium) are grouped with the latter.

## CHAPTER XXX

### CARBON AND CARBON COMPOUNDS

#### **CARBON**

##### OFFICIAL FORMS OF CARBON

*Activated Charcoal*, U. S. P. XIII

*Purified Animal Charcoal*, N. F. VIII

Symbol, C. Valence, IV. Atomic Weight, 12.010;  
Atomic Number, 6

**Occurrence.**—This non-metallic element is found in the free condition as the diamond in Brazil, Venezuela, India and South Africa, as graphite (plumbago) in the United States, Germany, Spain, Siberia, Canada, Ceylon and Bohemia, and as coal which is very widely distributed.

Carbon is the fundamental constituent of all animal and vegetable tissue and of coal and petroleum. In the form of carbonates, it enters the composition of many minerals such as chalk, dolomite, calcite, witherite, calamine, and spathic iron ore. Combined with oxygen it is found to a small extent as carbon dioxide in the atmosphere. In combination with hydrogen it occurs as methane or marsh gas.

**Allotropic Modifications.**—Carbon exists in two *crystalline* modifications, *viz.*, diamond and graphite. So-called "amorphous" carbon is in reality a mass of very minute crystals, which have the identical crystalline structure of graphite.

**Diamond.**—Diamond is the purest native form of uncombined carbon. It occurs in colorless, tinted or black crystals belonging to the regular system. Diamond has a density of 3.50 to 3.56. It is one of the hardest known substances (10 on Mohs' scale) and must be "cut" and polished with diamond dust. It has a high index of refraction (2.417 for sodium light). It is a good conductor of heat but a poor conductor of electricity. The diamond resists the action of most chemicals. When it is burned in oxygen, carbon dioxide and a trace of ash result.

Colorless or tinted diamonds are "cut" into those shapes that secure the greatest light reflection and refraction. When these are polished, they form gems having remarkable brilliance and luster. Black diamonds (carbonado) and those that cannot be cut into gems because of flaws, are used for cutting glass or for pointing rock drills.

Artificial diamonds of microscopic size were prepared by Moissan in 1893 by suddenly cooling molten iron containing dissolved carbon and then dissolving the iron in acid.

*Graphite.*—This variety of crystalline carbon occurs native in Ceylon, the United States, Germany, Spain, Siberia, and elsewhere. Its physical properties are markedly different from those of diamond. It is a soft, unctuous, black or dark lead-colored, shiny solid which is composed of crystalline scales belonging to the hexagonal system. It has a density of 2.09 to 2.23 and is a good conductor of electricity. Like diamond, it resists the action of chemicals at ordinary temperatures. When heated in oxygen, it is converted into carbon dioxide.

Large quantities of artificial graphite are now being manufactured by the Acheson process at Niagara Falls.

Graphite is very soft and leaves a black mark on paper and other objects when drawn across them, hence the name "graphite" from the Greek meaning "to write." "Lead" pencils are made by squirting a paste of powdered graphite and varying quantities of grit-free clay through perforated plates. The small rods of "lead" are dried, cut into desired lengths and baked to remove all moisture. They are then glued in wooden cases.

Because intense heat does not affect graphite, it is used to make stove polish and protective paints. It is also employed for making electrodes for use in electro-chemical industries. Crucibles, (plumbago crucibles) made from graphite and clay are used in making crucible steel (*q. v.*).

The unctuous property of graphite, together with its great resistance to heat, makes it suitable as a lubricant for machinery running at high temperatures. Unlike lubricating oils, graphite is not absorbed by wood, and therefore is used to reduce the friction between moving wooden parts of machines.

*Coal.*—These natural deposits are the result of slow decomposition of vegetable matter in the presence of water, the absence of air, and under pressure. Coal consists of carbon, carbon compounds, mineral matter, and moisture. There are many varieties of coal but only two general kinds, *viz.*, *anthracite* or *hard* coal and *bituminous* or *soft* coal. The former contains about 90 per cent of carbon and about 6 per cent of volatile matter. It ignites with some difficulty and burns without appreciable smoke or flame, giving off a large quantity of heat. It is used extensively for domestic heating purposes, for making producer gas, and in electric furnace reductions. Bituminous or soft coal contains about 70 per cent of carbon with large quantities of volatile matter. Soft coal burns with a smoky flame. Soft coal is used for both domestic and industrial heating and for the manufacture of illuminating gas and coke.

*Other Forms of Carbon.*—There are numerous other kinds of carbon, *e. g.*, (1) charcoal, (2) lampblack and carbon black, (3) coke and (4) gas carbon. These forms of carbon are amorphous and are obtained by the destructive distillation of many carbon compounds. The various kinds of amorphous carbon differ greatly as to purity and physical properties; their properties depending upon the substances from which they are made. As previously stated,

none of these well-known forms is *pure* carbon because they contain variable amounts of other elements or their compounds.

**Physical Properties.**—1. *Activated Charcoal*, U. S. P. XIII.—It is a fine, black, odorless, tasteless powder free from gritty matter. When dried to constant weight at 120° C. it loses not more than 15 per cent of its weight. Upon incineration the residue does not exceed 4 per cent of its weight.

2. *Purified Animal Charcoal*, N. F. VIII.—It occurs as a dull black, amorphous, odorless, and tasteless powder, which burns with a red glow but without a flame. When dried at 105° C. for five hours, it loses not more than 12 per cent of its weight.

Both forms of carbon are insoluble in water and all common organic solvents. They have adsorbing properties for gases and for solids, *e. g.*, coloring matter and alkaloids, in solution. The activated charcoal is the better adsorbent.

Wood charcoal is characterized by its power to adsorb various gases. One volume at 0° C. and 760 mm. pressure will adsorb 171.7 cc. of ammonia, 86.3 cc. of nitrous oxide, 67.7 cc. of carbon monoxide, 21.2 cc. of carbon dioxide, 17.9 cc. of oxygen, 15.2 cc. of nitrogen and 4.4 cc. of hydrogen. The adsorptive power of charcoal is dependent upon its porosity.

**Chemical Properties.**—1. *Activated Charcoal*.—The aqueous filtrate from a boiled suspension is colorless and neutral to litmus paper.

2. *Purified Animal Charcoal*.—When boiled with water the filtrate is neutral to litmus.

Both official forms of carbon exhibit the chemical properties of carbon. At ordinary temperatures, carbon is an inactive element, but its activity rapidly increases with rising temperatures until, at about 3500° C., it becomes very active. At elevated temperatures, it has a great affinity for oxygen and forms carbon dioxide and carbon monoxide. The different forms of carbon are variously affected by the most active oxidizing agents (*e. g.*, nitric acid and potassium chlorate). For example, diamond is scarcely attacked by them, graphite is but slowly oxidized, and charcoal is rapidly oxidized. At the temperature of the electric furnace, carbon unites with many metals and some non-metals to form carbides, such as calcium carbide ( $\text{CaC}_2$ ), aluminum carbide ( $\text{Al}_4\text{C}_3$ ), and silicon carbide or carborundum ( $\text{SiC}$ ), etc. When heated with the various metallic oxides, *e. g.*, zinc oxide, copper oxide, iron oxide, etc., carbon reduces them to the metal and carbon monoxide, carbon dioxide, or a mixture of the two, depending upon the amount of charcoal used. Carbon will unite with hydrogen in the presence of finely divided nickel at a temperature of 250° C. to form methane ( $\text{CH}_4$ ). A number of molten metals will dissolve at least small quantities of carbon, which generally cause a deterioration in metallicity. Iron, however, gains in elasticity and tensile strength with only slight loss of plasticity.

**Official Tests for Identity.**—1. *Activated Charcoal*. 2. *Purified Animal Charcoal*. The official compendia do not provide specific tests for their identification. All of the monograph requirements lend themselves to identifying the carbon preparation. A distinction can be made between the two official forms when all of the monograph requirements are compared.

**Commercial Manufacture.**—1. *Activated Charcoal*.—This form of carbon is obtained by the destructive distillation of plant substances. The materials mostly used are wood,<sup>1</sup> waste liquor from wood pulp, paper, molasses, fruit stones, nut shells, corn cobs and straw. An activated form of charcoal may be produced by (1) mixing pumice with the plant material and distilling, (2) adding a salt such as zinc chloride and distilling at a low temperature, or (3) by heating carbon at high temperatures in the presence of steam.

2. *Purified Animal Charcoal*.—Bones are first boiled with water under pressure to extract the gelatin, and then destructively distilled in iron retorts. A vile-smelling liquid called "bone oil" or Dippel's oil passes over and a residue of carbon and calcium phosphate remains. This form of carbon is very impure because it contains approximately 83 per cent of calcium phosphate. On account of its great decolorizing and adsorbing powers, it is used extensively by sugar refiners. Crude animal charcoal is never used in medicine or in the decolorization of acid solutions until it has been purified by repeatedly digesting it with boiling dilute hydrochloric acid and then thoroughly washing it. The method for its preparation is given below.

Another charcoal of animal origin is made by calcining a mixture of fresh blood and potassium carbonate in large cylinders. The product is purified by boiling with diluted hydrochloric acid and subsequently reheating the washed charcoal.

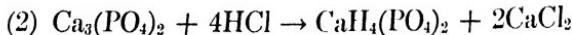
The property possessed by animal charcoal of being a remarkable decolorizing agent is due to the extensive internal surface of the material and therefore, its increased surface attraction. Organic coloring matters, such as litmus, indigo, certain colored resins, etc., may be removed from solution by proper treatment with charcoal.

**Laboratory Preparation of Purified Animal Charcoal.**—Introduce 100 Gm. of animal charcoal, No. 60 powder, into a capacious flask (1500 cc.) provided with a one-hole rubber stopper and 5 feet of 1 cm. glass tubing to act as a reflux. Add 200 cc. of hydrochloric acid and 400 cc. of boiling water. By means of a sand bath keep the mixture boiling gently for eight hours, adding water from time to time to maintain the original volume. Then add 500 cc. of boiling water, transfer the mixture to a muslin strainer and, when the liquid has run off, return the charcoal to the original flask. Now add 200 cc. of boiling water and 100 cc. of hydrochloric acid and boil for two hours. Again add 500 cc. of boiling water and transfer the whole to a plain filter. When the liquid has drained off, wash

<sup>1</sup> Chem. Ind., 60, 80 (1947).

the charcoal with boiling water until the washings give only a faint cloudiness with silver nitrate test solution. Dry the product in an oven and immediately transfer it to a well-stoppered bottle.

When bone black is digested with hydrochloric acid, the insoluble calcium phosphate that it contains is converted into soluble calcium phosphate and calcium chloride which then may be washed out (2).



**Pharmaceutical Preparations and Uses.**—1. *Activated Charcoal* (*Carbo Activatus*), U. S. P. XIII.—Activated Charcoal is the residue from the destructive distillation of various organic materials, treated to increase its adsorptive power.

Permission is given by the U. S. P. to dispense activated charcoal whenever *Carbo Ligni* is prescribed. It is used for its adsorptive properties in the treatment of stomach and intestinal disorders where gases, chemicals, enzymes or toxins are to be removed. When wet, activated charcoal will not adsorb gases and therefore its use for "gas on the stomach" is irrational. Charcoal chewing gums have not been accepted by the A. D. A. as dental remedies.<sup>1</sup>

2. *Purified Animal Charcoal* (*Carbo Animalis Purificatus*), N. F. VIII.—Purified Animal Charcoal is charcoal prepared from bone and purified by removing the substances which are dissolved by hot hydrochloric acid and water. It is used for treating the same conditions as is activated charcoal but it is less adsorptive. Average dose—0.3 Gm. (approximately 5 grains).

#### NON-OFFICIAL FORMS OF CARBON

1. *Lampblack and Carbon Black*.—Lampblack may be prepared by burning oil, tar, resin, turpentine or other rich carbonaceous substances in an insufficient supply of air. The products of combustion are collected on cloths suspended in condensing chambers. Lampblack is usually made by allowing the luminous flame of burning oil to play upon a water-cooled rotating iron disk. The deposited soot (lampblack) is removed with a scraper. *Carbon black* is made by burning natural gas with an insufficient amount of air. Large quantities of both lampblack and carbon black are made by the pyrolysis of hydrocarbons (see p. 32). Lampblack and carbon black are used in making printer's ink, black paints and varnishes, rubber goods and in calico printing.

2. *Coke*.—This form of carbon is a grayish, porous solid, which burns with very little flame and no smoke. It is made by driving off the volatile matter from bituminous coal. This operation is still carried on to a very limited extent in fire-brick ovens shaped like beehives. The ovens are filled with coal which is partly burned to raise the temperature. All air is then shut off and the heat destructively distills the rest of the coal. The yield of these beehive ovens is about 65 per cent of coke, but all of the valuable by-products,

<sup>1</sup> J. A. Ph. A. Pr. Ed., p. 370, August (1946.)

*e. g.*, ammonia, organic compounds, tar, and combustible gases (illuminating gas) are lost. Therefore, the beehive ovens have been largely replaced by the more modern *by-product coke ovens*. These ovens not only permit the saving of the volatile products but also increase the coke yield by about 10 per cent. Coke is used for fuel, for the reduction of iron ore to pig iron, and for many other industrial purposes.

3. *Gas Carbon*.—This is a by-product of the manufacture of illuminating gas. It is a black, dense, hard form of carbon. It is a good conductor of electricity and therefore is used for making carbon electrodes, etc.

### CARBON COMPOUNDS

The natural and synthetic compounds of carbon already described in the literature number well over 500,000 and are more numerous than the known compounds of any other element. This vast number is not difficult to account for when one considers that carbon derivatives are the chief components of all plants and animals. The natural sources of carbon compounds quite logically lead to the use of the name *organic* to differentiate them from *inorganic* or mineral substances. Carbon compounds bear a definite relationship to one another but differ markedly in general behavior from the compounds of other elements. In fact, they form a distinct group, the consideration of which constitutes the interesting study of *Organic Chemistry*. Only a few of the simpler compounds of carbon will be considered here.

### CARBON AND HYDROGEN

Compounds composed only of hydrogen and carbon are known as *hydrocarbons*. The hydrocarbons may be *saturated* or *unsaturated* compounds. The simplest saturated hydrocarbon is *methane* ( $\text{CH}_4$ ) and the simplest unsaturated hydrocarbon known is *acetylene* ( $\text{C}_2\text{H}_2$ ). Both saturated and unsaturated hydrocarbons form *homologous series* in which the individual compounds, when arranged in the order of their molecular weights, differ from the compounds immediately preceding and following them by a definite increment, *e. g.*,  $\text{ClH}_2$ . At ordinary temperatures, carbon and hydrogen do not unite. In the presence of a contact agent (finely divided nickel) and at a temperature of  $250^\circ \text{ C}$ ., powdered carbon will combine with hydrogen to form methane ( $\text{CH}_4$ ). When hydrogen is passed through an electric arc formed between carbon poles, some acetylene ( $\text{C}_2\text{H}_2$ ) is produced.

### OFFICIAL COMPOUND OF CARBON AND CHLORINE

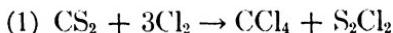
#### *Carbon Tetrachloride*, N. F. VIII

Formula,  $\text{CCl}_4$ . Molecular Weight, 153.84

Carbon Tetrachloride or tetrachlormethane ( $\text{CCl}_4$ ) is a clear, colorless, mobile liquid having a characteristic odor resembling that

of chloroform. It boils between 76° and 78° C., has a specific gravity of not less than 1.588 and not more than 1.590 at 25° C., and is an excellent solvent for fats, tars, most fixed and volatile oils, and many organic compounds. It is soluble in about two thousand times its volume of water and is miscible with alcohol, with chloroform, with ether, with benzene, and with petroleum benzin. It is non-inflammable. It is slowly decomposed by light, and by various metals, if moisture is present.

Carbon tetrachloride is made by passing dry chlorine into carbon disulfide containing a small quantity of iron as catalyst (1).



The carbon tetrachloride is first distilled off at 77° C. and the sulfur monochloride (boiling-point, 136° C.) is rectified for industrial use.

Carbon tetrachloride is used **with caution** as an anthelmintic. The average adult dose (single dose) is 2.5 cc. (approximately 40 minimis). The N. F. VIII recognizes the *Carbon Tetrachloride Capsules* (*Capsulae Carbonei Tetrachloridi*). These capsules must contain not less than 92 per cent and not more than 108 per cent of the labeled amount of  $\text{CCl}_4$ . The capsules usually available contain 1 cc. (approximately 15 minimis) of Carbon Tetrachloride.

When a sufficient quantity of carbon tetrachloride is added to benzine, the mixture becomes non-inflammable and as such is used as a safe solvent for the removal of spots and stains from clothing, etc. It is also used to kill moths.

Carbon tetrachloride is the main constituent of many fire extinguishers. When the liquid is sprayed upon burning material, the temperature is lowered due to the heat consumed in vaporizing the carbon tetrachloride and these same vapors exclude the air and thus stop combustion.

## OFFICIAL COMPOUNDS OF CARBON AND OXYGEN

### CARBON DIOXIDE

#### *Carbon Dioxide*, U. S. P. XIII

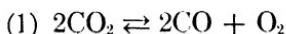
Formula,  $\text{CO}_2$ . Molecular Weight, 44.01

**Physical Properties.**—Carbon dioxide is a colorless, odorless gas. An aqueous solution of the gas has a faintly acid taste. It is about one and a half times heavier than air, 1 liter weighing 1.977 Gm. at 760 mm. and at 0° C. At 25° C. and 760 mm. pressure, it is soluble in about its own volume of water. For pressures up to about 4 atmospheres, the gas conforms to Henry's law.<sup>1</sup> By subjecting the gas to a pressure of about 59 atmospheres, it is rather easily converted into a colorless liquid which freezes at -57.7° C.

<sup>1</sup> The concentration of a saturated solution of a given gas is proportional to the concentration of pressure at which the gas is supplied.

The vapor pressure of solid carbon dioxide is 760 mm. at  $-79^{\circ}\text{C}.$ , hence upon exposure to air the solid evaporates without melting. The rapid evaporation of liquid carbon dioxide (from cylinders) absorbs sufficient external heat to convert the remainder to a crystalline mass (carbon dioxide "snow"). It is used to produce low temperatures. So-called "dry ice" is  $\text{CO}_2$ -snow pressed into forms.

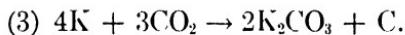
**Chemical Properties.**—As evidenced by the extinguishing of a burning taper in the gas (air containing 2.5 per cent of  $\text{CO}_2$ ), carbon dioxide does not support combustion. Between  $1200^{\circ}\text{ C.}$  and  $1300^{\circ}\text{ C.}$ , it is slightly decomposed into carbon monoxide and oxygen (1).



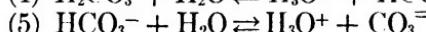
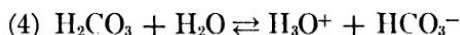
At  $2000^{\circ}\text{ C.}$ , 1.8 per cent of carbon dioxide is decomposed. It will be noted that the reaction is a reversible one and, therefore, the products of the decomposition reunite when the temperature is lowered. However, in the presence of a combustible substance, all of the carbon dioxide is reduced to monoxide. Burning magnesium ribbon continues to burn in an atmosphere of carbon dioxide, reduces the latter to carbon and forms the oxide of the metal (2).



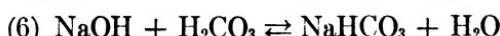
When carbon dioxide is passed over heated sodium or potassium, the carbonates of the metals and carbon are formed (3).



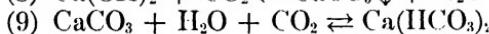
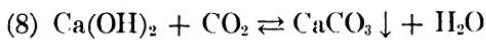
*Carbonic Acid and Its Salts.*—As previously stated, carbon dioxide is soluble in water and produces a liquid which contains the very weak acid known as carbonic acid. This acid reddens blue litmus paper and is a very poor conductor of electricity. Being a dibasic acid, it characteristically ionizes in steps, although the secondary ionization is very slight (4) and (5).



Carbonic acid forms both acid (hydrogen) and normal salts. Thus, when carbon dioxide is passed into a solution of a fixed alkali, the hydrogen salt or bicarbonate is formed (6) which, contrary to expectations, does not give an acid solution because of the small ionization of the  $\text{HCO}_3^-$ . When an equivalent amount of fixed alkali is added to a solution of the bicarbonate, the normal carbonate is formed (7). Due to the somewhat reversible character of this reaction, solutions of alkali carbonates are alkaline in reaction.



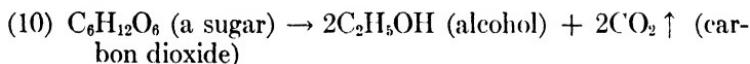
The carbonates and bicarbonates of ammonium and the alkali metals are soluble, whereas the carbonates of other metals are almost insoluble. When carbon dioxide is passed into a solution of calcium hydroxide (lime water) or barium hydroxide (baryta water), a white precipitate of calcium or barium carbonate is formed (8) (test for  $\text{CO}_2$ ). If an excess of carbon dioxide is employed, the precipitates dissolve because of the formation of the respective hydrogen carbonates or bicarbonates (9). Thus, when a natural water containing carbon dioxide in solution trickles over limestone (normal calcium carbonate), some of the latter is dissolved as calcium bicarbonate (see Temporary Hard Water, p. 50). If the solution is heated, carbon dioxide is evolved and the normal calcium carbonate is reprecipitated (9).



**Official Tests for Identity.**—1. Carbon dioxide extinguishes a flame (*q. v.*).

2. A precipitate of barium carbonate is formed when the gas is passed through a solution of barium hydroxide (8).

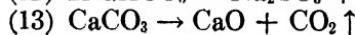
**Commercial Manufacture.**—Carbon dioxide occurs in small quantities in the atmosphere (about 0.03 to 0.04 per cent), in the earth, and in the waters of some springs and wells. Some gas wells produce gas which is nearly pure carbon dioxide. It is invariably produced when any compound containing carbon (*e. g.*, wood, coke, coal, oil, gas, etc.) is burned in excess of oxygen. Carbon dioxide is one of the products of chemical change (*e. g.*, decay, fermentation) in organic matter (10). Carbon dioxide is also formed by the slow combustion of foods in the body (digestion).



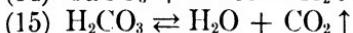
**Preparation.**—1. When coke is burned in air, an impure gas containing nitrogen results. When this product is forced under pressure into a concentrated solution of potassium carbonate, only the carbon dioxide is absorbed forming potassium bicarbonate (11). When the pressure is reduced and the solution heated, carbon dioxide, free from nitrogen, is obtained (11). The carbon dioxide under high pressure may be dissolved in cold water to form  $\text{H}_2\text{CO}_3$ . When the pressure is released the carbon dioxide is again liberated. This is compressed in iron cylinders.



2. Carbon dioxide may be obtained by heating sodium bicarbonate (12). A large number of normal carbonates are also decomposed by heat to oxide and carbon dioxide (13).



3. When a carbonate is treated with an acid, carbon dioxide is evolved. This method is employed for generating carbon dioxide for laboratory use. Calcium carbonate (small lumps of marble) is placed in a Kipp generator and dilute hydrochloric acid is allowed to act upon it (14). The unstable carbonic acid produced by the reaction immediately decomposes into water and carbon dioxide (15).



**Pharmaceutical Preparations and Uses.**—1. *Carbon Dioxide* (Carbonei Dioxidum, Carbonic Acid Gas), U. S. P. XIII.—Carbon Dioxide contains not less than 99 per cent by volume of CO<sub>2</sub>. For convenience it is usually supplied in compressed form in metallic cylinders.

Inhalations of oxygen containing 5 per cent of carbon dioxide are efficacious in the treatment of poisoning by carbon monoxide, alcohol, methanol, morphine and, in fact, all cases of depressed respiration (anesthesia accidents, etc.). The carbon dioxide stimulates the vasomotor as well as the respiratory center.



FIG. 18. Treatment of angioma on the eyelid with a dry ice pencil is safe because the dry ice is confined in the applicator and chips cannot fall into the eye. (Photograph, courtesy of the Kidde Manufacturing Company, Inc.)

Carbon dioxide is used in the manufacture of various chemicals, *viz.*, sodium bicarbonate (baking soda), normal sodium carbonate (washing soda), basic lead carbonate (white lead), etc. Soda water (carbonated water) is made by charging water with the gas under a pressure of 3 to 4 atmospheres. When carbonated water is administered orally, it hastens absorption in the stomach, increases the secretion of acid gastric juice (Chiari, 1915) and acts as a carminative.

tive. It is used to relieve nausea. It is used pharmaceutically to mask the disagreeable taste of certain medicines.

Carbon dioxide snow for correcting many skin disorders has been known as an effective remedy since its introduction in 1905 by Pusey.<sup>1</sup> It has been used successfully in the treatment of such skin conditions as acne, angiomas, corns and callouses, eczema, moles, psoriasis and warts. A convenient apparatus for making small quantities of carbon dioxide snow is now available.<sup>2</sup>

#### NON-OFFICIAL COMPOUNDS OF CARBON AND OXYGEN

**Carbon Monoxide.**—Carbon monoxide is a colorless gas having a very faint pungent odor and a slightly metallic taste. It is only slightly soluble in water (3 cc. in 100 cc. water at about 0° C., 760 mm.) with which it does not form a compound. Liquid carbon monoxide boils at -193° C. and freezes at about -200° C.

Carbon monoxide is an unsaturated compound and therefore combines directly with oxygen, chlorine and the metals (*viz.*, nickel, iron), to form additive products. At high temperatures, carbon monoxide has a great affinity for combined oxygen (oxides), a fact that is utilized in the recovery of the various metals from their respective ores. Because of the increasing number of accidental and suicidal deaths due to carbon monoxide poisoning, this compound is of great toxicological interest. The affinity of hemoglobin for carbon monoxide is said to be about two hundred and ten times greater than it is for oxygen. Thus, a very low concentration of carbon monoxide in the air (0.2 to 0.4 per cent) is generally fatal. It produces a very stable, cherry-red "carbonic oxide hemoglobin," which prevents the hemoglobin from uniting with oxygen (oxyhemoglobin) and asphyxia results. Asphyxia produced by carbon monoxide is the same as ordinary asphyxia, except that the skin and mucous membranes are colored a bright red due to CO-hemoglobin instead of being cyanotic (blue), a fact of great diagnostic importance. The treatment consists of artificial respiration or forced inhalations of oxygen, and warmth. Blood transfusions also have proven very efficacious. Fifty cc. intravenous injections of a 1 per cent methylene blue<sup>3</sup> (methylthionine chloride) solution are claimed by some to be a valuable adjunct to the above measures. Within recent years, a large number of deaths has resulted from carbon monoxide produced by allowing automobile engines to run in poorly ventilated garages.

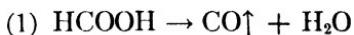
This gas constitutes 4 to 10 per cent of ordinary *coal* or *illuminating gas* and 30 to 40 per cent of *water gas* (*q. v.*). It is their principal toxic constituent.

<sup>1</sup> J. Am. Med. Assn., **49**, 1954 (1907).

<sup>2</sup> Central Scientific Company, Chicago 13, Illinois

<sup>3</sup> South. Med. J., **27**, 812 (1934).

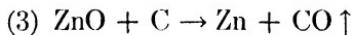
*Preparation.*—1. Carbon monoxide may be prepared in the laboratory by heating formic acid or a formate with concentrated sulfuric acid and collecting the gas over water (1).



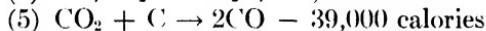
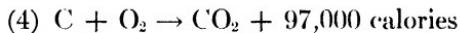
When oxalic acid or an oxalate is heated with concentrated sulfuric acid, both carbon monoxide and carbon dioxide are formed (2). The mixture is then passed through a solution of sodium hydroxide which combines with the carbon dioxide to form sodium carbonate and permits the unchanged monoxide to be collected over water.



2. Carbon monoxide is produced when many metallic oxides are reduced with carbon (3) (coke or charcoal).

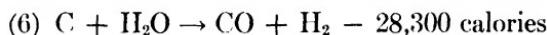


3. When the oxygen of the air comes in contact with hot carbon, carbon dioxide is formed (4). The carbon dioxide is readily reduced by subsequent contact with hot carbon to carbon monoxide (5).



4. When air is forced through or passed over hot coke, a mixture of carbon monoxide (1 part by volume) and nitrogen (3 parts by volume) called *producer gas*, is formed. If air and steam together are forced through hot carbon, the product contains hydrogen as well as carbon monoxide and nitrogen and is known as *modified producer gas*.

5. Water gas is essentially a mixture of carbon monoxide (about 45 per cent) and hydrogen (about 50 per cent). When steam is forced through incandescent coke, carbon monoxide and hydrogen are formed. Because of the endothermal character of the reaction (6), the coke becomes too cool to react. Therefore, an air-blast is substituted for the steam and this soon causes the coke to become incandescent and ready to again react with steam.



When a mixture of steam and air is passed through incandescent coke, the product is called *semi-water gas*. The oxygen of the air unites with the coke to produce a temperature sufficiently high to permit of the formation of water gas.

Because of the ease of manufacture, the uniform burning qualities and the rather high heat values, these gases are used extensively as a fuel for industrial and domestic purposes.

#### NON-OFFICIAL COMPOUNDS OF CARBON AND SULFUR

**Carbon Disulfide** ( $\text{CS}_2$ , 76.12).—Carbon disulfide is a clear, colorless, highly refractive, very volatile, inflammable liquid boiling at

about 46° C. and having a specific gravity of 1.26 at 25° C. An explosive mixture is formed when CS<sub>2</sub> vapors are mixed with air. It is slightly soluble in water and very soluble in alcohol, ether, chloroform and fixed or volatile oils. It readily dissolves sulfur, rubber, iodine and phosphorus.

Carbon disulfide is made<sup>1</sup> by direct union of sulfur vapor and glowing charcoal. The vapors of carbon disulfide are condensed in a suitable apparatus. Commercially, it is used as a solvent, particularly in the rubber industry.

<sup>1</sup> Am. Prof. Pharm., p. 379 (January 1946).

## CHAPTER XXXI

### SILICON AND SILICON COMPOUNDS

#### SILICON

Symbol, Si. Valence, IV. Atomic Weight, 28.06;  
Atomic Number, 14

**History and Occurrence.**—Silicon was discovered by Berzelius in 1823. This non-metallic element does not occur in the uncombined condition in Nature. In combination with other elements it is, with the exception of oxygen, the most widely distributed and abundant of all the elements. When united with oxygen as silicon dioxide (silica), it occurs in the form of quartz, flint, sand, etc. In this form or in that of the silicates, it is the principal constituent of nearly all rocks and likewise of the soil resulting from their disintegration. Silica is found also in the normal ashes of many plants, in the feathers of birds and in the hairs of animals.

**Physical Properties.**—Silicon exists in two allotropic forms: the *amorphous* and the *crystalline*. *Amorphous* silicon is a dark brown powder having a density of 2.35. When heated to dull redness in an atmosphere of oxygen, it burns with a brilliant flame and forms the dioxide. *Crystalline* or semi-metallic silicon occurs as large, silvery octahedral crystals having a density of 2.49. It melts at 1420° C. and boils at about 2600° C. It will scratch glass. Unlike the amorphous variety, it does not inflame in oxygen even when heated to a white heat. It burns in chlorine or fluorine.

**Chemical Properties.**—It resists attack by all acids except hydrofluoric, which, when mixed with nitric acid and heated, slowly dissolves it. Hot concentrated solutions of sodium or potassium hydroxides dissolve silicon with the evolution of hydrogen (1).



Silicon is tetravalent in all of its compounds. Chemically, it closely resembles carbon with which it unites at the temperature of the electric furnace to form compounds that are known as silicides, *e. g.*, carbon silicide (carborundum CSi).

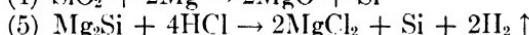
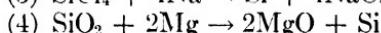
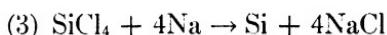
At red heat, silicon decomposes ammonia into hydrogen and a compound containing silicon and nitrogen. Silicon reduces many metallic and non-metallic oxides. When fused with alkaline carbonates and hydroxides, it is converted into silicon dioxide which dissolves in the molten alkali to form soluble alkali silicates.

**Tests for Identity.**—The element, silicon, can be recognized by its physical and chemical properties. Silicates can be identified by first converting them into silicon dioxide by fusion with a mixture of sodium and potassium carbonates and then digesting the mass

first, with hot water and then with hydrochloric acid. The thoroughly washed precipitate of  $\text{SiO}_2$  is then warmed in a lead or platinum dish with calcium fluoride and sulfuric acid (hydrofluoric acid may be used) and the gaseous silicon tetrafluoride ( $\text{SiF}_4$ ) passed into water in which it hydrolyzes into gelatinous silicic acid and fluosilicic acid (2).



**Commercial Manufacture.** - 1. *Amorphous silicon* may be prepared by (a) the reduction of  $\text{SiCl}_4$  with sodium at a high temperature (3) and (b) by heating powdered sand with magnesium powder (4) and then digesting the mass with hydrochloric acid (5) to remove magnesium oxide and any magnesium silicide ( $\text{Mg}_2\text{Si}$ ); (c) it is also prepared by reducing  $\text{SiO}_2$  in an electric furnace with coke. The temperature is very carefully controlled.



2. *Crystalline silicon* may be prepared by dissolving amorphous silicon in molten zinc and allowing the melt to cool slowly. The zinc is removed by treatment with hydrochloric acid.

It may be made either by reducing  $\text{Na}_2\text{SiF}_6$  or  $\text{SiO}_2$  with an excess of Al, or by heating  $\text{SiO}_2$  with carbon in an electric furnace.

**Pharmacological Action of Soluble Silicates.** —Very small quantities of silicates are found in nearly all tissues. When orally administered, soluble silicates act as mild alkalies. Soluble sodium silicate (water glass) is readily absorbed from the alimentary tract and is excreted by the urine. Large doses cause lesions of the capillaries with interstitial inflammation of the organs, especially the liver. Cases of acute poisoning by sodium silicate have been reported.

Intravenous injections of sodium silicate produce intravascular coagulation of the blood.

**Uses.** —Silicon is used in the manufacture of silicon tetrachloride (*q. v.*) and various alloys, *e. g.*, silicon bronze (composed of copper, tin and silicon and used for telephone and telegraph wires), ferro-silicon, etc. Silicon (also ferrosilicon) is sometimes used in the production of hydrogen for filling balloons.

When coke, silica and ferric oxide ( $\text{Fe}_2\text{O}_3$ ) are heated together in an electric furnace, a gray, crystalline compound known as *ferro-silicon* is formed. This alloy of iron and silicon is used in making special steels (*e. g.*, duriron, corrosiron, etc.) which are very resistant to the action of acids (especially nitric acid). Silicon and ferro-silicon are used as "scavengers" (*q. v.*) in the steel industry.

#### OFFICIAL COMPOUNDS OF SILICON

**Purified Siliceous Earth, *Terra Silicea Purificata*, U. S. P. XIII.** — Purified Siliceous Earth is a form of silica ( $\text{SiO}_2$ ) consisting of the

frustules and fragments of diatoms, purified by boiling with diluted hydrochloric acid, washing, and calcining. It is also known as purified kieselguhr, purified infusorial earth, purified tripoli, etc.

It is an amorphous, very fine, white, light gray or pale buff powder. It is gritty, readily absorbs moisture, and retains about four times its weight of water without becoming fluid. Purified siliceous earth is insoluble in water, acids, or in dilute solutions of the alkali hydroxides. It does not lose more than 10 per cent of its weight upon ignition. It is used in pharmacy as an absorbent and clarifying agent. Silica is used as a polishing powder for metals and for making scouring soaps, soluble glass, cement and dynamite (nitroglycerin absorbed in siliceous earth and moulded into sticks).

**Pharmaceutical Preparations.**—1. *Zinc Oxide Hard Paste* (Pasta Zinc Oxidi Dura, Unna's Hard Zinc Paste), N. F. VIII.—This paste contains 5 per cent purified siliceous earth as a stiffening agent.

*Bentonite*.—(See p. 437.)

*Kaolin*.—(See p. 438.)

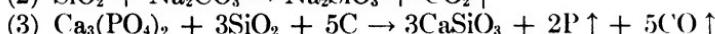
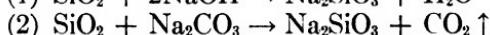
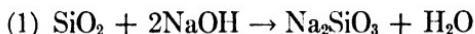
*Pumice*.—(See p. 440.)

*Talc*.—(See p. 367.)

## NON-OFFICIAL SILICON COMPOUNDS

**Silicon Dioxide or Silica** ( $\text{SiO}_2$ ).—In the free condition and also combined with metallic oxides, this compound occurs widely and abundantly distributed in Nature. Pure silica is known in both the crystalline and amorphous forms. *Quartz* (nearly pure  $\text{SiO}_2$ ), *tridymite* and *cristobalite*, are examples of the former. Quartz is the best known of these crystalline varieties of silica. Quartz specimens that are colored with various impurities are often used as gems, *e. g.*, amethyst (containing manganese and iron). Tridymite and cristobalite are not as common as quartz and differ from it in crystallographic structure. Amorphous silica is found in Nature as agate, jasper, carnelian, etc. Opal and flint are natural hydrated silicon dioxides.

Amorphous silica can be obtained by fusing a finely powdered silicate with sodium carbonate, decomposing the soluble sodium silicate thus formed with hydrochloric acid, evaporating the solution to dryness in order to convert the silicic acid into silica and washing the residue free from soluble chlorides with hot water. The white, amorphous powder thus obtained is insoluble in water and all acids (except hydrofluoric). It dissolves in hot solution of caustic alkalies (1) and to a lesser extent in alkali carbonates (2). At high temperatures  $\text{SiO}_2$  acts as a strong acid, replacing the  $\text{P}_2\text{O}_5$  in normal tricalcium phosphate (3), etc.



Both the crystalline and amorphous forms of silica melt from 1600° to 1700° C. and boil at 2230° C., but the amorphous form sublimes at 1750° C. When pure silica (rock crystal) is fused in an electric furnace whose carbon electrodes are protected from the sticky melt with carbonized paper, the viscous material can be drawn into threads or moulded into flasks, crucibles, dishes, tubes, etc. These products are translucent and because of the very small cubical coefficient of expansion ( $5 \times 10^{-7}$ ) possessed by the material from which they are made, will not break when they are heated red hot and plunged into cold water. This variety of fused silica is known as *vitreosil*. When fragments of quartz are fused under pressure in an electric furnace, a transparent quartz is obtained which can be rolled into sheets or made into optical lenses that will withstand intense heat. Because such a clear, fused quartz interposes less resistance than glass to the passage of light through it (especially the beneficial ultra-violet of sunlight), it is used in making window panes for use in hospitals, etc.

The use of sandstone and quartzite for building purposes is well known. Enormous quantities of sand are used in making glass, porcelain, china, cement, water glass, sand paper, etc.

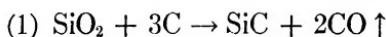
Glass does not possess any crystalline structure nor definite melting-point and therefore, may be considered to be a super-cooled liquid. It is essentially a mixture of various silicates. The basic elements are usually alkali or alkaline earth oxides, and metallic oxides, whereas silicon dioxide usually constitutes the acidic constituent. Other acid-forming oxides such as boric oxide or phosphoric pentoxide are sometimes employed in whole or part. The physical properties of glass are dependent upon the basic and acidic oxides used in its preparation. Thus, ordinary *soft glass* (readily softened by heat) is a fusion product of lead silicate ( $Pb_2SiO_5$ ) and sodium silicate ( $Na_2SiO_3$ ), whereas, *hard glass* contains potassium silicate and sometimes magnesium or aluminum oxides in place of sodium silicate. A glass having low refraction but high dispersion is called a *flint glass*. A lead-potassium glass is an example. It is used in making lenses for optical instruments, cut glass dishes, etc. A *crown glass* has a high refraction and a low dispersion. Lead and barium glasses are examples. Soda lime glass is used for common bottles. A very tough glass having a much lower coefficient of expansion than ordinary glass is made by heating together a large excess of silica with borax, sodium oxide, and aluminum oxide. This glass does not crack when exposed to sudden changes in temperature and therefore is used for making chemical glassware (pyrex, containing up to 80 per cent silica) and certain cooking utensils.

The very chemical nature of glass suggests that under suitable conditions it might hydrolyze to a slight degree and yield free hydroxide ion, silicon dioxide, or some of the polysilicic acids. Soft glass, especially, is prone to such decomposition. Therefore, the National Formulary VIII establishes tests for solubility and reac-

tion as a minimum requirement of quality of the glass that is to be used for the manufacture of ampuls.

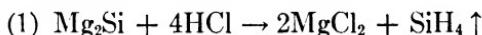
**Silicon Carbide.**—Carborundum ( $\text{SiC}$ , 40.07).—Pure silicon carbide forms green to bluish-black, iridescent, crystalline plates belonging to the hexagonal system. The commercial product has a hardness of 9.5 which is between that of sapphire and diamond. It fuses with difficulty, but decomposes at about  $2200^\circ \text{ C}$ . Its specific gravity is 3.17 at  $20^\circ \text{ C}$ . It resists attack by almost all chemical reagents.

It is made by Acheson's process, which consists in heating a mixture of coke, sand and a little sawdust and salt in an electric furnace (1). The resistance offered to a powerful electric current by a core of granular carbon is sufficient to raise the temperature to about  $1950^\circ \text{ C}$ . At this temperature, the silicon unites chemically with the carbon and carbon monoxide is given off.



Because of its extreme hardness, pulverized silicon carbide is mixed with a binder (clay) and moulded into whetstones, grindstones, etc. The powdered material is used as an abrasive.

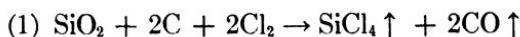
**Hydrides.**—Just as carbon forms series of hydrocarbons, so silicon forms at least one series having the general formula  $\text{Si}_n\text{H}_{2n+2}$ , which corresponds to the methane or paraffin series. At least the first five or six members of this series have been prepared; the two best known ones are monosilane ( $\text{SiH}_4$ ) and disilane ( $\text{Si}_2\text{H}_6$ ). The former may be prepared by treating magnesium silicide (made by fusing a mixture composed of anhydrous magnesium chloride, dried  $\text{Na}_2\text{SiF}_6$ ,  $\text{NaCl}$ , and  $\text{Na}$ ) with water or acids (1).



Monosilane is a colorless gas which, when pure, does not spontaneously inflame at ordinary temperatures and pressures. However, when prepared as given above, it is contaminated with small amounts of disilane (silicoethane) and then ignites spontaneously, evolving dense fumes of silicon dioxide. It burns in chlorine to form chlorine derivatives.

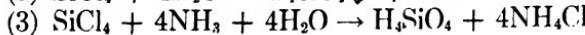
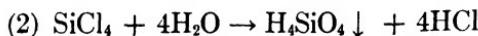
Disilane may be prepared by treating lithium silicide with concentrated hydrochloric acid. It burns in air and behaves as a reducing agent.

**Halogen Compounds.**—**Silicon Tetrachloride** ( $\text{SiCl}_4$ , 169.888) is formed when a current of chlorine is passed over a hot mixture of silica and carbon (1). The vapors are condensed in an ice-cooled vessel.



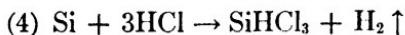
It is a clear, colorless, stable, fuming liquid which boils at  $57.5^\circ \text{ C}$ . and has a specific gravity of 1.52 at  $0^\circ \text{ C}$ . Water decomposes it into silicic acid and hydrochloric acid (2). It unites with ammonia

to form a dense, white smoke which consists of silicic acid and ammonium chloride (3). It is used in warfare to produce a *smoke screen*, and in the glass and ceramic industries.



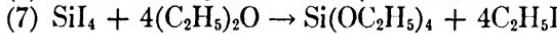
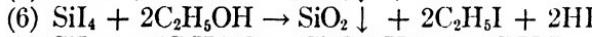
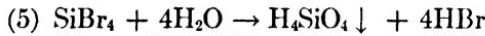
**Silicon Hexachloride** ( $\text{Si}_2\text{Cl}_6$ ) is formed when vapors of silicon tetrachloride are passed over fused silicon. It is a colorless, fuming liquid that boils at about  $146^\circ \text{ C}$ . It is decomposed by water.

**Silicon Chloroform** ( $\text{SiHCl}_3$ ).—This compound is analogous to chloroform ( $\text{CHCl}_3$ ). It is formed when crystallized silicon is heated to dull redness in hydrogen chloride (4).

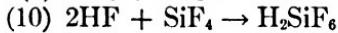
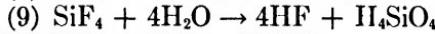
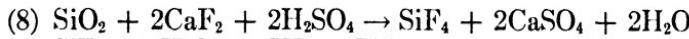


It is a colorless, fuming liquid that boils at  $33^\circ \text{ C}$ . It burns with a greenish flame and is decomposed by water. **Silicon bromoform** ( $\text{SiHBr}_3$ , melting-point  $60^\circ \text{ C}$ .) and **silicon iodoform** ( $\text{SiHI}_3$ , melting-point  $8^\circ \text{ C}$ .) have also been prepared.

**Silicon Tetrabromide** ( $\text{SiBr}_4$ , 347.72) and **Silicon Tetraiodide** ( $\text{SiI}_4$ , 535.74) are made by methods that are similar to those used in preparing the tetrachloride. The bromide is a colorless liquid that boils at about  $153^\circ \text{ C}$ ., whereas the iodide crystallizes in colorless octahedra which melt at  $120^\circ \text{ C}$ . and boil at  $290^\circ \text{ C}$ . Both compounds are decomposed by water (5), alcohol (6), and ether (7) with great evolution of heat.



**Silicon Tetrafluoride** ( $\text{SiF}_4$ ) is prepared by heating silica with fluorspar and concentrated sulfuric acid (8). It is a colorless gas having a very pungent odor. It is decomposed by water into orthosilicic acid (9) ( $\text{H}_4\text{SiO}_4$ ) and fluosilicic acid (10) ( $\text{H}_2\text{SiF}_6$ ).



**Fluosilicic Acid and Fluosilicates.**—When the vapor of silicon tetrafluoride is brought in contact with water, a vigorous reaction takes place with the formation of silicic acid (insoluble) and fluosilicic acid (soluble). (See Silicon Tetrafluoride.) In order to prevent stoppage of the tube with the gelatinous silicic acid, the end is kept under mercury upon which is superimposed a layer of water. When the solution is filtered and concentrated, the fluosilicic acid decomposes into silicon tetrafluoride and hydrofluoric acid (11).

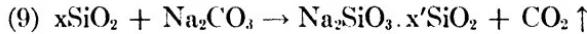


A fluosilicate is formed by neutralizing a solution of fluosilicic acid with a base. Most of these salts are soluble but others, notably those of lithium, potassium, sodium, barium, and calcium are almost insoluble. Fluosilicates which are used for insect powders and insecticide sprays have been shown by Marcovitch to be very toxic.

**The Silicic Acids.**--When silicon tetrachloride is treated with water, orthosilicic acid ( $H_4SiO_4$ ) is thrown down as a gelatinous precipitate which is a good example of a *hydrogel* or *gel*. Orthosilicic acid, formed by the interaction of sodium silicate (dilute solution) and hydrochloric acid, remains in the colloidal state and is known as a *hydrosol* or *sol*. Orthosilicic acid cannot be prepared from its anhydride (silicon dioxide) and water, but must be made as previously described. When 1 molecule of orthosilicic acid loses a molecule of water, it is converted into metasilicic acid ( $H_2SiO_3$ ). A number of other silicic acids in the form of their simple or mixed salts are found in Nature. These acids may be considered as condensed or polysilicic acids and are formed by the loss of water from more than 1 molecule of orthosilicic acid (1 to 8).

- (1)  $H_4SiO_4$  (zircon— $ZrSiO_4$ ; garnet— $Ca_3Al_2(SiO_4)_3$ )
- (2)  $H_4SiO_4 - H_2O \rightarrow H_2SiO_3$  (metasilicic acid) (enstatite— $MgO \cdot SiO_2$ ; beryl— $3BeO \cdot Al_2O_3 \cdot 6SiO_2$ )
- (3)  $2H_4SiO_4 - H_2O \rightarrow H_6Si_2O_7$  (orthodisilicic acid) (kaolinite— $Al_2Si_2O_7 \cdot 2H_2O$ ; hardystonite— $Ca_2ZnSi_2O_7$ )
- (4)  $2H_4SiO_4 - 2H_2O \rightarrow H_4Si_2O_6$  (dimetasilicic acid) (rhodonite— $Mn_2Si_2O_6$ ; spodumene— $AllLiSi_2O_6$ )
- (5)  $2H_4SiO_4 - 3H_2O \rightarrow H_2Si_2O_5$  (metadisilicic acid) (rivaite— $Ca_2Na_2(Si_2O_5)_3$ )
- (6)  $3H_4SiO_4 - 2H_2O \rightarrow H_8Si_3O_{10}$  (orthotrisilicic acid) (melilithe— $Ca_4Si_3O_{10}$ )
- (7)  $3H_4SiO_4 - 3H_2O \rightarrow H_6Si_3O_9$  (trimetasilicic acid) (wollastonite— $Ca_3Si_3O_9$ )
- (8)  $3H_4SiO_4 - 4H_2O \rightarrow H_4Si_3O_8$  (trisilicic acid) (meerschaum— $Mg_2Si_3O_8 \cdot 2H_2O$ ; orthoclase— $AlKSi_3O_8$ )

*Water glass* is made by fusing sand (silica) with sodium carbonate (9).



Water glass is not pure sodium (meta) silicate. By varying the quantities of silica and sodium carbonate in the fusion mixtures, products containing silicates of variable compositions and of different solubilities are obtained. Commercial solutions of water glass are sometimes called "silicate of soda." These are of variable composition and contain an excess of silica, most of which is in colloidal suspension. Such solutions are used for glueing cardboard boxes and for "filling" cheap soaps. Silicate of soda is employed as a fire-proofing agent for wood, cloth, fiber, board, etc. Dilute solutions are used for preserving eggs. A granular powder of the

hydrated sodium metasilicate ( $\text{Na}_2\text{SiO}_3 \cdot 5\text{H}_2\text{O}$ ) is used as a detergent.

Soluble sodium silicate and also colloidal silicic acid have been recommended for the treatment of tuberculosis and arteriosclerosis. They have not been established clinically.

When an alkaline solution containing about 20 per cent of sodium silicate is exposed to the air, it forms a hard, glassy mass. Fracture dressings are sometimes coated with this solution.

**Salts of Polysilicic Acids.**—Purified forms of native aluminum polysilicate (kaolinite,  $\text{Al}_2\text{Si}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$ ) and of native magnesium polysilicate (talc,  $\text{Mg}_3\text{H}_2(\text{SiO}_3)_4$ ) are recognized by the N. F. VIII and the U. S. P. XIII, respectively.

## CHAPTER XXXII

### TITANIUM, ZIRCONIUM AND CERIUM AND THEIR COMPOUNDS

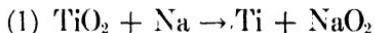
#### TITANIUM

Symbol, Ti. Valence, II, III, IV. Atomic Weight, 47.90; Atomic Number, 22

IN 1789, the Rev. William Gregor discovered a new metal in *ilmenite* ( $\text{FeTiO}_3$ ). Six years later Klaproth studied the composition of *rutile* and named the metal it contained, *titanium*. Subsequently, he found the same metal in *ilmenite*. The name of the element signifies the "sons of the earth."

According to Clarke's table of the abundance of the elements, titanium stands just above chlorine. It occurs in a greater amount than either phosphorus or carbon. It is found as the dioxide,  $\text{TiO}_2$ , in the minerals *rutile*, *brookite* and *anatase*, all three possessing different crystalline forms. Another important mineral is *ilmenite*. Magnetic iron ores frequently contain titanium.

The metal is difficult to obtain in the pure state. Its dioxide is reduced by sodium or magnesium (1).



Podszus describes a method of making almost pure titanium by heating the tetrachloride with sodium in a steel bomb filled with hydrogen or carbon dioxide (2).



Titanium is a steel-gray, brittle metal having a density of 4.87. It melts at about  $1800^{\circ}\text{C}$ . It burns brilliantly in oxygen and unites with nitrogen with great vigor. Its alloys with steel are of some importance.

#### OFFICIAL COMPOUNDS OF TITANIUM

#### TITANIUM DIOXIDE

*Titanium Dioxide*, N. F. VIII

Formula,  $\text{TiO}_2$ . Molecular Weight, 79.90

**Physical Properties.**—Titanium Dioxide occurs as a white, amorphous, tasteless, odorless, infusible powder. A suspension of titanium dioxide (1 in 10) in distilled water is neutral to litmus paper. It is insoluble in water, in hydrochloric acid, in nitric acid, and in dilute sulfuric acid.

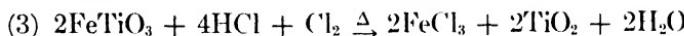
**Chemical Properties.**—Titanium dioxide dissolves in hot concentrated sulfuric acid, and in hydrofluoric acid. It is rendered soluble by fusion with potassium bisulfate or with alkali hydroxides or carbonates.

Hydrogen peroxide reacts with titanium dioxide in dilute sulfuric acid to produce an orange-red color of titanium peroxide ( $TiO_3$ ).

The dioxide is reduced to metallic titanium when heated with carbon, calcium, sodium or magnesium.

**Official Tests for Identity.**—Titanium dioxide is dissolved in sulfuric acid with the aid of heat. This solution is diluted and filtered. An orange-red color of titanium peroxide develops upon the addition of a few drops of hydrogen peroxide.

**Commercial Preparation.**—Titanium dioxide occurs in Nature (*q. v.*) but a better product is obtained by treating ilmenite ( $FeTiO_3$ ) with hydrogen chloride and chlorine (3).



**Pharmaceutical Preparations and Uses.**—1. *Titanium Dioxide* (*Titanii Dioxidum*), N. F. VIII.—“Titanium Dioxide, when dried at  $105^\circ$  for 3 hours, contains not less than 99 per cent of  $TiO_2$ .” It is used as a white pigment in creams and paints. The refractive characteristic makes it useful to ward off light rays and is used for this purpose in sun-tan preparations. It does not react with hydrogen sulfide, is very stable to weather conditions and spreads well when mixed with a suitable paint base. These properties make it useful for special paints.

2. *N. F. Sun Cream* (*Cremor Solis N. F.*, Sun Tan Ointment), N. F. VIII.—This cream contains 1 per cent of titanium dioxide as a refractory material.

#### NON-OFFICIAL COMPOUNDS OF TITANIUM

**Compounds.**—The main valence of Titanium is 4. It exhibits also the valence of 2 and 3. Thus the oxides  $TiO$  and  $Ti_2O_3$  are known. The peroxide,  $TiO_3$ , has been obtained. The chlorides  $TiCl_2$  and  $TiCl_3$  are powerful reducing agents.  $TiCl_4$  hydrolyzes very readily and, being a liquid, fumes strongly in moist air. The sulfates  $Ti(SO_4)_2$  and  $TiSO_4$  have been prepared. In addition to acting as a metal in the foregoing compounds, titanium acts as a non-metal to form titanates such as  $K_2TiO_3$  and  $CaTiO_3$ . The latter compounds occur in the Urals and in Arkansas as the mineral *perofskite*.

#### ZIRCONIUM

Symbol, Zr. Valence, II, IV. Atomic Weight, 91.22; Atomic Number, 40

In 1789, Klaproth discovered a new earth in the mineral *zircon* to which he assigned the name “zirconia.” The metal was first prepared by Berzelius as a gray powder by heating potassium zircono-

fluoride with potassium. The metal was obtained in a state of purity of a little more than 99 per cent by heating the oxide,  $ZrO_2$ , with shavings of calcium in an evacuated vessel. Zirconium has a density of 6.4 and melts at about  $1927^\circ C$ .

**Compounds.**—Zirconium is found in Nature as the silicate, *zircon* ( $ZrSiO_4$ ) and as the oxide, *baddeleyite* ( $ZrO_2$ ). Zirconia,  $ZrO_2$ , is obtained from zircon,  $ZrSiO_4$ , by heating the latter with potassium hydrogen fluoride. Potassium zirconofluoride,  $K_2ZrF_6$ , is formed. This compound is decomposed with sulfuric acid and the zirconia is precipitated with ammonium hydroxide from the resulting solution. The oxide is both basic and acidic. It dissolves in acids to form salts such as the nitrate,  $Zr(NO_3)_4$ , and the sulfate,  $Zr(SO_4)_2$ . When the oxide is fused with basic oxides or carbonates of the metals, zirconates are formed. Meta- and ortho-zirconates such as  $Na_2ZrO_3$  and  $Na_4ZrO_4$  are known. Polyzirconates also have been prepared. The metal acts almost entirely with the valence of 4, yet the oxide,  $Zr_2O_3$ , and the hydride,  $ZrH_2$ , are given in the literature. Their existence is questionable. It acts like silicon by forming compounds such as  $K_2ZrO_6$ . The halides, such as  $ZrCl_4$ , hydrolyze easily to form basic salts, such as  $ZrOCl_2$ .

**Uses.**—Zirconium or its salts have found little use in medicine. Recently<sup>1</sup> it has been recommended for use in sutures and dental equipment because it does not corrode easily.

### CERIUM

Symbol, Ce. Valence, III, IV. Atomic Weight, 140.13;  
Atomic Number, 58

**History.**—In 1803, Berzelius and Hisinger simultaneously discovered the oxide ( $CeO_2$ ) of a new element in a Swedish mineral. Hisinger called the oxide *ceria* and the element *cerium* in allusion to the planet, Ceres, which had but recently been discovered. Mosander obtained the element in 1826, and found that *ceria* was a mixture of the oxides of cerium, lanthanum and "didymium."

**Occurrence.**—Cerium, together with lanthanum, praseodymium, neodymium, illinium and samarium, is found as silicate in the minerals *cerite* and *allanite*. The mineral *monazite*, which is the chief source of thorium oxide, also contains cerium.

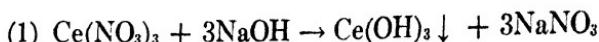
**Physical Properties.**—Cerium is an iron-gray, ductile and malleable metal. It has a density of 6.9, fuses at  $640^\circ C$ ., and boils at  $1400^\circ C$ . The metal is insoluble in water but soluble in acids.

**Chemical Properties.**—Cerium forms two series of compounds: (1) cerous salts ( $CeX_3$ ) and (2) ceric salts ( $CeX_4$ ).

The cerous salts are colorless and stable. In these cerium has a valence of 3. A cerous salt heated with a volatile acid such as nitric or oxalic, results in the formation of cerium dioxide ( $CeO_2$ ). The cerous oxide ( $Ce_2O_3$ ) may be obtained by reducing the dioxide

<sup>1</sup> Ind. Eng. Chem., 39, 34A (1947).

with calcium. Solutions of cerous salts, when treated with an alkali, form a white precipitate of cerous hydroxide (1).



This hydroxide is readily oxidized on exposure to air, to red, violet and finally yellow ceric hydroxide ( $\text{Ce(OH)}_4$ ). From solutions of cerous salts, ammonium sulfide precipitates cerous sulfide which is immediately hydrolyzed to the hydroxide.

The ceric salts color their solutions an orange-red. They are readily reduced by most reducing agents such as ferrous salts and hydroquinones to cerous salts. Ceric salts form insoluble carbonates and hydroxides.

**Commercial Manufacture.**—Metallic cerium is obtained with a small amount of lanthanum and other rare-earths mixed with it, by the electrolysis of cerium chloride. It may also be made by the reduction of the oxide with magnesium powder.

**Pharmacological Action of Cerium Ion.**—Cerium salts injected intravenously depress the heart and thus affect the circulation. When soluble salts are ingested they cause blood to effuse from the wall of the stomach and intestine. The use of insoluble salts such as cerium oxalate caused no effect since they are unabsorbed.

**Uses.**—Metallic cerium finds little use as such and is employed mostly for preparing its salts.

Cerium (about 70 per cent) and iron (about 30 per cent) form one of the principal *pyrophoric* alloys. It is often called "*misch metal*." When particles of this alloy are torn off by a file, they catch fire in the air and will ignite illuminating gas and vapors of benzine, alcohol, etc.; hence the use of this alloy in making gas lighters, cigar lighters, etc.

#### OFFICIAL COMPOUNDS OF CERIUM

##### CERIUM OXALATE

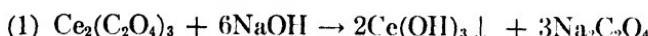
*Cerium Oxalate*, N. F. VIII

Formula,  $\text{Ce}_2(\text{C}_2\text{O}_4)_3$ . Molecular Weight, 544.26

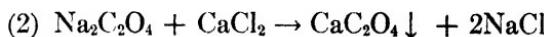
**Physical Properties.**—Cerium oxalate occurs as a fine, white, or slightly pink powder, without odor or taste, and is permanent in the air. It is insoluble in water, in alcohol, in ether, in solutions of the alkali hydroxides, in cold dilute sulfuric acid, and in cold dilute hydrochloric acid, but it is dissolved by these acids when heated.

**Chemical Properties.**—Cerium oxalate is the oxalate salt of *cerous* cerium, having the formula  $\text{Ce}_2(\text{C}_2\text{O}_4)_3$ .

1. Cerium Oxalate when treated with sodium hydroxide T.S. forms insoluble cerous hydroxide and soluble sodium oxalate (1).



When calcium chloride T.S. is added to the filtrate a white precipitate forms, insoluble in acetic acid but soluble in hydrochloric acid (2).



2. When a hot hydrochloric acid solution of cerium oxalate is treated with sodium hydroxide T.S. there is produced a white precipitate ( $\text{Ce}(\text{OH})_3$ ) that slowly turns yellow ( $\text{Ce}(\text{OH})_4$ ) (*q. v.*).

3. Ammonium carbonate T.S. when added to a hydrochloric acid solution of cerium oxalate causes white cerous carbonate to precipitate.

4. When the oxalate is ignited, it decomposes and leaves not less than 47 per cent of a reddish-brown residue. Cerium dioxide is white if pure but a brown color is due to the presence of praseodymium oxide ( $\text{Pr}_2\text{O}_3$ ).

5. When cerium oxalate is mixed with lead dioxide and the mixture boiled with nitric acid, the liquid becomes yellow due to the formation of ceric nitrate ( $\text{Ce}(\text{NO}_3)_4$ ).

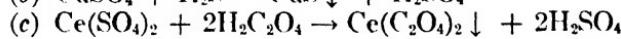
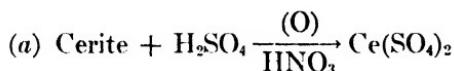
**Official Tests for Identity.**—1. Sodium hydroxide T.S. reacts with cerium oxalate to form soluble sodium oxalate that responds to the tests for the oxalate ion (*q. v.*).

2. Cerium oxalate in hot hydrochloric acid solution will produce a white precipitate ( $\text{Ce}(\text{OH})_3$ ) which slowly turns yellow in air ( $\text{Ce}(\text{OH})_4$ ).

3. A white precipitate ( $\text{Ce}_2(\text{CO}_3)_3$ ) is formed when ammonium carbonate T.S. is added to a hydrochloric acid solution of the salt.

**Commercial Manufacture.**—Cerium oxalate for medicinal use is prepared from the mineral cerite or from monazite sands by a rather lengthy process. The different steps involved are as follows: (a) Digestion of the powdered mineral with sulfuric acid and the oxidation of the dried mass with nitric acid. (b) Removal of copper and other heavy metals with hydrogen sulfide. (c) Precipitation of the cerite metals with oxalic acid. (d) Calcination of the mixed oxalates with magnesium carbonate and the solution of the residue in a small amount of nitric acid. (e) Precipitation of yellow ceric sulfate by pouring the nitric acid solution into a large volume of 0.5 per cent sulfuric acid and thus effecting a fair separation of cerium from other associated metals. (f) Solution of the ceric sulfate in sulfuric acid and its reduction with sodium thiosulfate to cerous sulfate. (g) Precipitation with oxalic acid of the cerous ion as oxalate and drying.

The following chemical equations possibly represent the chemical steps in the process.

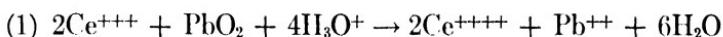


- (d)  $\text{Ce}(\text{C}_2\text{O}_4)_2 + 2\text{MgCO}_3 \xrightarrow{\Delta} \text{Ce}(\text{CO}_3)_2 + 2\text{MgO} + 3\text{CO}_2 \uparrow + \text{CO} \uparrow$   
 (e)  $\text{Ce}(\text{CO}_3)_2 + 4\text{HNO}_3 \rightarrow \text{Ce}(\text{NO}_3)_4 + 2\text{CO}_2 \uparrow + 2\text{H}_2\text{O}$   
 (f)  $\text{Ce}(\text{NO}_3)_4 + 2\text{H}_2\text{SO}_4 \rightarrow \text{Ce}(\text{SO}_4)_2 \downarrow + 4\text{HNO}_3$   
 (g)  $2\text{Ce}(\text{SO}_4)_2 + 2\text{Na}_2\text{S}_2\text{O}_3 \rightarrow \text{Ce}_2(\text{SO}_4)_3 + \text{Na}_2\text{S}_4\text{O}_6 + \text{Na}_2\text{SO}_4$   
 (h)  $\text{Ce}_2(\text{SO}_4)_3 + 3\text{H}_2\text{C}_2\text{O}_4 \rightarrow \text{Ce}_2(\text{C}_2\text{O}_4)_3 \downarrow + 3\text{H}_2\text{SO}_4$

**Pharmaceutical Preparations and Uses.**—1. *Cerium Oxalate* (*Cerii Oxalas*), N. F. VIII.—Cerium Oxalate is a mixture of the oxalates of cerium, neodymium, praseodymium, lanthanum, and other associated elements. It is used against vomiting, especially during the early stages of pregnancy. It has been found<sup>1</sup> that large doses, which are non-toxic, delay vomiting from local gastric irritation. The properties are similar to the insoluble bismuth compounds but have no advantage over them. Average dose—0.2 Gm. (approximately 3 grains).

#### NON-OFFICIAL COMPOUNDS OF CERIUM

**Ceric Sulfate.**—Ceric sulfate,  $\text{Ce}(\text{SO}_4)_2$ , contains variable amounts of water. It also contains sulfates of the other associated earths. It occurs as yellow to orange-yellow crystals or as a crystalline powder. The salt is insoluble in cold water, slowly soluble in cold dilute mineral acids and readily soluble when heated with these solvents. It is a strong oxidizing agent and may replace potassium permanganate in most reactions. The salt must be used in acid solutions as it hydrolyzes to ceric hydroxide in neutral or basic solutions. The ceric salt may be prepared from the cerous salt by (a) heating with lead dioxide ( $\text{PbO}_2$ ) and nitric acid (1) (see Chemical Property 5), (b) heating with ammonium persulfate, (c) electrolysis, (d) treating with sodium bismuthate. Ceric sulfate is used in U. S. P. XIII as an oxidizing agent in the assay of mass of ferrous carbonate, menadione, and tablets of ferrous sulfate.



**Other Compounds.**—Cerium forms two basic oxides,  $\text{Ce}_2\text{O}_3$  and  $\text{CeO}_2$ . The dioxide is used extensively in making gas mantles which, when heated by the non-luminous flame of a burner, become incandescent and emit a white light. These mantles usually contain about 1 per cent of cerium dioxide and 99 per cent of thorium dioxide.

**Cerous Nitrate** [ $\text{Ce}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ ] crystallizes in colorless, transparent prisms. It may be made by the mutual decomposition of cerous sulfate and barium nitrate. *Ceric nitrate* [ $\text{Ce}(\text{NO}_3)_4$ ], like all of the ceric salts, is orange-red in color.

<sup>1</sup> Baehr and Wessler (1909).

## CHAPTER XXXIII

### GERMANIUM AND TIN AND THEIR COMPOUNDS

#### GERMANIUM

Symbol, Ge. Valence, II, IV. Atomic Weight, 72.60; Atomic Number, 32

**History and Occurrence.**—In 1871, Mendeléeff predicted this element and gave it the name *eka-silicon*. Winkler discovered it in 1886 in the mineral *argyrodite* (5 to 7 per cent Ge), which is a sulfide of germanium and silver ( $\text{GeS}_2 \cdot 3\text{Ag}_2\text{S}$ ) mined at Freiburg, Saxony, and Ormo, Bolivia. He found the properties of this new element to be in close agreement with those predicted by Mendeléeff for the hypothetical element, *eka-silicon*. It is also found in *euxenite* in Sweden.

**Physical Properties.**—Germanium is a soft, white, lustrous metal. It has a density of 5.36 and melts at  $958.5^\circ\text{C}$ . When the fused metal is slowly cooled, it crystallizes in the regular system. It is stable in air.

**Chemical Properties.**—The metal is insoluble in hydrochloric acid. It is readily attacked by nitrohydrochloric and sulfuric acids to form  $\text{GeCl}_4$  and  $\text{Ge}(\text{SO}_4)_2$ , respectively. Nitric acid oxidizes the element to white germanic oxide ( $\text{GeO}_2$ ). It is insoluble in concentrated solutions of the alkali hydroxides but dissolves with incandescence in molten alkali hydroxides.

Germanium forms two series of compounds. In one of these the metal is bivalent (germanous series) and in the other quadrivalent (germanic series). It unites directly with the halogens.

Germanium forms two oxides,  $\text{GeO}$  and  $\text{GeO}_2$ , from which are derived two series of compounds, *viz.*, the germanous and the germanic. Germanous compounds are rather unstable, whereas the germanic compounds are characterized by their greater stability. *Germanous chloride* ( $\text{GeCl}_2$ ) is a strong-smelling liquid obtained by heating the metal in an atmosphere of hydrogen chloride. It boils at  $72^\circ\text{C}$ . *Germanic chloride* ( $\text{GeCl}_4$ ) is a liquid resembling germanous chloride. It is made by the action of chlorine upon the metal. It boils at about  $86^\circ\text{C}$ ., and is easily hydrolyzed by water.

Germanium salts give almost no characteristic reactions with the different reagents. In general behavior, it lies between tin and silicon. White germanic sulfide ( $\text{GeS}_2$ ) is precipitated by hydrogen sulfide from strongly acid solutions of germanium salts. The precipitate is soluble in ammonium sulfide.

**Commercial Manufacture.**—The pulverized mineral, *argyrodite* (approximately 5 to 7 per cent of germanium) is thoroughly mixed with equal weights of sodium carbonate and sulfur and then fused. When cooled, the mass is extracted with water in which the ger-

manium goes into solution as a thio-compound. The arsenic and antimony are separated by neutralizing the solution with sulfuric acid. The filtered solution is made distinctly acid with hydrochloric acid and the germanium precipitated with hydrogen sulfide as white germanic sulfide ( $\text{GeS}_2$ ). The metal is obtained either by reducing the sulfide with hydrogen, or the oxide,  $\text{GeO}_2$ , with hydrogen, carbon or magnesium.

**Uses.**—Germanium dioxide has been used to increase the formation of red blood cells, and for the treatment of anemia. It is not in general use.

### TIN

Symbol, Sn. Valence, II, IV. Atomic Weight, 118.70;  
Atomic Number, 50

**History.**—This element is found as a component of prehistoric bronzes and therefore must have been used by man as a metal many thousands of years before the dawn of history.<sup>1</sup> In his writings, Herodotus spoke about the Cassiterides or "tin islands." It is evident that tin was imported from the British Isles (Cornwall) into Italy after, if not before, the conquest of Britain by Julius Caesar. Pliny's writings indicate that in his time the Romans did not differentiate between tin and lead, because he refers to the former as *plumbum album* and to the latter as *plumbum nigrum*.

**Occurrence.**—Small quantities of the free metal are found in the gold ores of Siberia, Guiana and Bolivia. The principal ore of tin is *cassiterite* or *tinstone*, which is almost pure, crystallized  $\text{SnO}_2$ . It occurs in its matrix in veins or disseminated through rock masses and is known as *vein-* or *mine-tin*. The disintegration of these rocks gives rise to alluvial gravels (found in stream-beds) in which *tinstone* is found in the form of lumps or grains and is called *stream-tin*. Most of the tinstone is obtained from the Malay Peninsula, the islands of Banka and Billiton, the Dutch East Indies, Bolivia, Cornwall, and Australia. In the United States, tin is found in South Dakota and in South Carolina.

**Physical Properties.**—At ordinary temperatures, tin is a white, lustrous metal having a density of 7.31 and a crystalline form belonging to the tetragonal system. It is a good conductor of heat and electricity. It is pliable and malleable, and may be rolled into very thin sheets (tin-foil). When tin is bent, a peculiar sound is heard. This is sometimes called the "cry of tin," and is caused by the friction of its crystalline particles. At  $161^\circ \text{ C}$ . *tetragonal tin* changes to *rhombic tin*, which is brittle and has a density of 6.56. *Rhombic tin* melts at  $231.9^\circ \text{ C}$ . and distils at  $2270^\circ \text{ C}$ . The transition of *tetragonal tin* to *gray tin* takes place either at low temperature ( $-40^\circ \text{ C}$ .) or when gray tin is present and, when the conversion is once initiated, it proceeds rapidly. The metal modifies its structure

<sup>1</sup> The early Greek alchemists named the metal Hermes and during the sixth century, it was called Zensor Jupiter and designated by the symbol R.

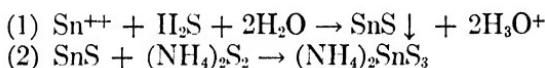
and becomes a gray powder having a specific gravity of 5.85 at 15° C. The transition temperature is 18° C., and the phenomenon is known as "tin-disease" or "tin-plague."

**Chemical Properties.**—At ordinary temperatures, tin is only slightly changed by air and by water. As the temperature is increased, a film of oxide ( $\text{SnO}$ ) forms on the surface, and at white heat the metal is converted to the dioxide ( $\text{SnO}_2$ ), which is yellow when hot and white when cold.

Tin is slowly attacked by dilute acids, yielding stannous salts and hydrogen. Concentrated nitric acid converts it into  $\beta$ -stannic acid (meta-stannic acid). The metal resists weak alkalies, but dissolves in hot concentrated alkalies to form meta-stannates and hydrogen.

Tin unites directly with most of the non-metals. It forms also a number of very useful alloys, *e. g.*, pewter (Sn, 80 per cent; Pb, 20 per cent), solder (Sn, 50 per cent; Pb, 50 per cent), type metal (Sn, 25 per cent; Pb, 50 per cent; Sb, 25 per cent), gun metal (Sn, 10 per cent; Cu, 90 per cent), Rose's metal (Sn, 25 per cent; Pb, 25 per cent; Bi, 50 per cent), bronze, bell metal, britannia metal, etc. Tin forms an amalgam which is used largely for silvering mirrors.

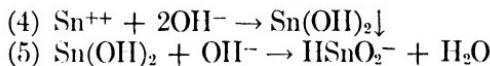
The chemical properties of the stannous and stannic ions are expressed in the following reactions. 1. When hydrogen sulfide is passed through a not too acid solution of a stannous salt, brown stannous sulfide (1) which is soluble in ammonium sulfide (2) is precipitated.



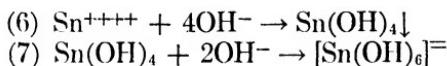
With a solution of a stannic salt, hydrogen sulfide precipitates yellow stannic sulfide, which is soluble in ammonium sulfide (3).



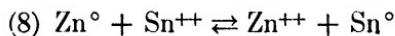
2. Sodium or potassium hydroxide added to a solution of a stannous salt, produces a white precipitate of stannous hydroxide (4), which is easily soluble in alkalies to form stannites (5).



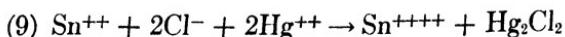
With stannic salts, the alkali hydroxides precipitate white stannic hydroxide (6) which is soluble in an excess of the alkali to form stannate (7).



3. When metallic zinc is placed in an acidified (HCl) solution of a tin salt, metallic tin is deposited (8).

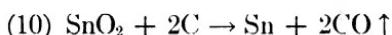


When tin is dissolved in boiling hydrochloric acid, the solution gives a white or gray precipitate with mercuric chloride test solution (9).

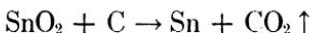


4. Acid tin solutions are reduced to stannous ion by the addition of aluminum or antimony. When a drop of this solution is added to a saturated aqueous solution of cacothelin<sup>1</sup> on drop-reaction paper, a violet to red coloration shows presence of tin.

**Commercial Manufacture.**—Cassiterite is crushed to a coarse powder and most of the gangue separated by gravity, flotation, or by magnetic methods. The “concentrated” ore, now containing from 83 to 88 per cent of  $\text{SnO}_2$ , is roasted in a furnace with a revolving hearth, during which operation the sulfur and arsenic are eliminated. The residue is usually lixiviated with water or a dilute muriatic acid to separate the iron, copper and bismuth. The washed material is mixed with powdered anthracite coal (10) and a little lime to facilitate the formation of a slag and reduced in a reverberatory furnace.



or



The impure tin that collects in a separate vessel at the bottom of the furnace is refined by *liquation*, repeated fusion, or electrolytically until a product of about 99.75 per cent purity is obtained. The *liquation* process consists in heating the ingots just sufficiently to melt the tin but not the more difficultly fusible metals (iron, copper, etc.). The tin is then “flowed off.” Tin is purified also by agitating the molten metal, skimming off the lighter impurities from the surface, and pouring off the purified tin from the heavier metals that settle on the bottom. Tin is sometimes purified by stirring the molten metal with sticks of green wood and skimming off the impurities that collect on the surface of the melt.

**Pharmacological Action of Tin Ion.**—Repeated oral administrations of tin salts result in the absorption of tin ion. Poisoning is rare because of the lack of cumulative tendency. When solutions of tin salts are hypodermically injected, they stimulate the central nervous system and paralysis subsequently takes place. The symptoms of tin poisoning resemble those of lead, *viz.*, inflammation of the stomach and intestines with marked injury to the kidneys and paresis of the heart. Tin is retained principally by the skin and the liver. Elimination slowly takes place by way of the alimentary tract and to a lesser degree by the kidneys.

Tin has a marked germicidal effect against staphylococci. It has been observed that persons who work in tin are rarely if ever afflicted with furunculosis. This has led to the use of metallic tin

<sup>1</sup> Spot Tests—Feigl, p. 63.

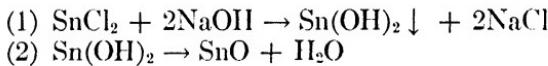
and also tin oxide in the treatment of acne, furunculosis, etc. Local applications of dilute solutions of the chloride are said to be of value in treating slow-healing infected wounds.

**Uses.**—On account of its resistance to very weak acids and alkalies, tin is used for household utensils, chemical apparatus (still coils), etc. *Tinplate* is employed in making "tin cans," etc. It is made by immersing thin sheets of iron that have been washed with hydrochloric or sulfuric acids in baths of molten tin. Fabricated articles of solid tin are said to be made of "block tin" in order to distinguish them from those made from tinplate. Tin is used in alloys (*q. v.*), solder, coins, piping, and for preparing tin salts. Metallic tin is incorporated in pills and tablets that are used for acne and furunculosis.

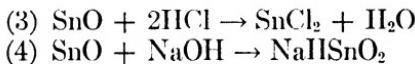
### COMPOUNDS OF TIN

Tin forms two series of compounds, *viz.*, *stannous*, in which the metal is bivalent, and *stannic*, in which the element is quadrivalent. Stannous compounds are readily changed into stannic compounds by oxidation, and consequently they are frequently used as reducing agents.

**Oxides.**—**Stannous Oxide** ( $\text{SnO}$ ).—An olive-green stannous oxide may be made by adding a strong base to a solution of a stannous salt (1) and heating the precipitated stannous hydroxide (2). It may be obtained also as a gray powder by heating the metal with an insufficient amount of air or in a current of carbon dioxide.

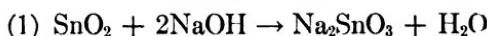


Stannous oxide is amphoteric. It dissolves in acids to give stannous salts (3) and in alkalies to form *stannites* (4).



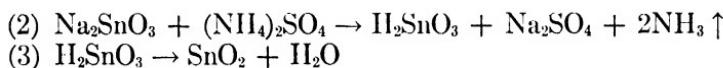
**Stannic Oxide** ( $\text{SnO}_2$ ).—Stannic oxide occurs in Nature as *cassiterite* (*q. v.*). It may be prepared by burning the metal in air or by igniting the hydroxide. It is a white, amorphous substance which is insoluble in acids or alkalies, and fuses at the temperature of the electric furnace. Its specific gravity is 7 at  $\frac{2}{4}\%$ . Stannic oxide is amphoteric; its acidic property, however, being more pronounced. It is the tin compound most commonly used in tablet form for internal administration. A 5 per cent tin oxide ointment is available for external use in staphylococci infections. Stannic oxide has been employed as the abrasive and polishing agent in dentifrices.

**Sodium Stannate.**—When stannic oxide is fused with alkalies, it forms soluble *stannates* (1), and thereby shows that quadrivalent tin usually acts as an acid-forming element.



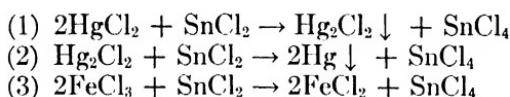
When a solution of sodium stannate is made slightly acid, there is precipitated a white, gelatinous  $\alpha$ -stannic acid ( $H_2SnO_3$ ) which readily dissolves in dilute acids and alkalies. When a hydrochloric acid solution of sodium stannate is allowed to stand,  $\beta$ -stannic acid (often called meta-stannic acid) is slowly deposited. It is formed also when tin is acted upon by nitric acid.  $\beta$ -stannic acid is thought to be a polymer of  $\alpha$ -stannic acid, but differs from the latter by being only slowly acted upon by alkalies and acids and by forming a different series of salts.

Solutions of sodium  $\alpha$ -stannate are frequently used to render cotton goods non-inflammable. The cloth is saturated first in the solution and then dried. Then it is soaked in a solution of ammonium sulfate (2) and after washing out the sodium sulfate and drying (3), the fibers are found to be impregnated with stannic oxide.



**Tin Proteinates.**—Tin combines with proteins to form insoluble tin complexes similar to those of silver, etc. Several such compounds are marketed for the internal administration of tin. One is a 6 per cent solution of sclero-sulphydryl proteins organically combined with tin for intramuscular use.

**Halogen Compounds.**—**Stannous Chloride** ( $SnCl_2$ ).—The anhydrous salt is made by subjecting heated tin to the action of hydrogen chloride. When tin is treated with the theoretical amount of hydrochloric acid, the dihydrate ( $SnCl_2 \cdot 2H_2O$ ) crystallizes out. This is known as *tin salt* and is used as a mordant. It loses its water at  $100^\circ C.$ , fuses at  $250^\circ C.$ , and distils at about  $606^\circ C.$ . Stannous chloride is a powerful reducing agent, converting mercuric chloride into mercurous chloride (1) or free mercury (2), ferric to ferrous salts (3), etc.



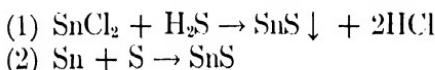
**Stannic Chloride** ( $SnCl_4$ ).—This fuming liquid, known as “fuming spirit of Libavius,” is made by the action of chlorine on tin or stannous chloride. It has a specific gravity of 2.23 at  $15^\circ C.$  and boils at  $115^\circ C.$  It dissolves in water with the evolution of a large amount of heat and, besides being definitely hydrolyzed, it forms several different hydrates, *viz.*, those containing 3, 4, 5, and 8 molecules of water. The pentahydrate is the best known and, because of its pasty consistency, is sold under the name “butter of tin” for mordanting and “loading” or “weighting” silk. Stannic chloride is almost completely hydrolyzed by water to hydrochloric acid and a hydrated stannic oxide (1).



When hydrogen chloride is passed through a cold solution of stannic chloride, chlorostannic acid crystallizes out as the hexahydrate ( $H_2SnCl_6 \cdot 6H_2O$ ). Ammonium chlorostannate [ $(NH_4)_2SnCl_6$ ] is known as "pink salt" and was used prior to the introduction of "butter of tin" for "loading" silk.

The bromides and iodides of stannous and stannic tin are known.

**Sulfides.**—**Stannous Sulfide** ( $SnS$ ).—Stannous sulfide is precipitated as a dark brown powder when hydrogen sulfide is passed into a solution of a stannous salt (1). It may be obtained as a gray crystalline mass by melting together tin and sulfur (2).



Stannous sulfide is insoluble in water and only very slightly soluble in ammonium monosulfide. It dissolves in polysulfides on heating to form thiostannates (3).



**Stannic Sulfide** ( $SnS_2$ ).—This compound is formed as a bright yellow precipitate when hydrogen sulfide is passed into a solution of stannic chloride (1).



It is insoluble in water and very dilute acids. Ammonium sulfide and sodium sulfide dissolve it to form thiostannates (2).



It is sometimes called "artificial gold" because of its golden yellow color.

## CHAPTER XXXIV

### LEAD AND LEAD COMPOUNDS

#### LEAD

Symbol, Pb. Valence, II, IV. Atomic weight, 207.21;  
Atomic Number, 82

**History.**—This metallic chemical element has been known since the earliest historic time. It is mentioned in the Old Testament (Job and Numbers). It was used extensively by the Romans for making conduits. Pliny describes a solder made of *plumbum nigrum* (lead) and *plumbum album* (tin), and it is quite evident that these two elements were considered as being varieties of the same substance. Dioscorides fully described a compound that evidently was litharge. White lead was known to Geber in the eighth century. Pliny called red lead by the name *minium*. As was the custom of the alchemists, this metal was associated with Saturn and designated by the sign of this planet.

**Occurrence.**—Very small quantities of uncombined lead are found in Nature. The principal lead ores are *galena* ( $PbS$ ), *cerusite* ( $PbCO_3$ ) and *anglesite* ( $PbSO_4$ ). Galena, the principal primary ore of lead, is by far the most important and widely distributed. It occurs in a great many geological formations, *e. g.*, veins in the cambrian clay slate, in beds or nests within sandstones and limestones, etc. Most of the galena that is connected genetically with igneous rocks is argentiferous or auriferous or both. The most important deposits of lead in the United States are located in Missouri, Oklahoma (Mississippi Valley District), Colorado, Nevada, Idaho and Utah (Rocky Mountain District). Lead ores are also mined in Cumberland and Cornwall, England, Wales, Scotland, Mexico, Germany, Austria and in the southern provinces of Spain.

Until the discovery of the large deposits of cerusite (native lead carbonate) in Colorado and Nevada, this ore was not considered of much metallurgical value. It is quite evident that originally this native carbonate was galena, as the latter is always present in admixture. The crude ore contains about 30 per cent of lead and from 0.2 to 2 per cent of silver.

Anglesite is a native lead sulfate and generally may be considered as an alteration product from galena. Large quantities are found in France, Spain, Sardinia and Australia. This ore is poor in silver and only occasionally is mined for itself.

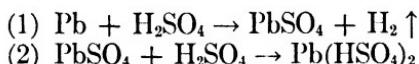
**Physical Properties.**—Lead is a bluish-gray, feebly lustrous metal, having a density of 11.34. It is very soft and plastic and hence may be cut or rolled with ease. It is nearly devoid of elasticity.

When warmed, lead is especially plastic and may be "squirted" through dies to form tubes or wire. While in this plastic condition it may be "wiped" on a connection of two pipes to form a joint. Lead crystallizes in two forms, *viz.*, octahedral and monoclinic. It melts at 327.43° C., vaporizes at a bright red heat and boils at a temperature of 1613° C. Lead readily forms alloys, the better known ones being solder, pewter, type metal, Rose's metal, Babbitt metal, etc.

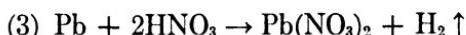
**Chemical Properties.**—1. *Metallic Lead.*—Lead tarnishes rapidly in moist air. When fused in the presence of air, it quickly forms lead monoxide ( $PbO$ ). The rate of this oxidation increases with the temperature. In the absence of air, pure water does not attack lead. However, when air is present, lead hydroxide [ $Pb(OH)_2$ ], which is appreciably soluble in water, is formed. The presence in water of bicarbonate ions or sulfate ions (hard water) effects the precipitation of any lead ions as an insoluble basic carbonate or sulfate which further inhibits the action of the water upon the metal. Lead pipes are dangerous to use as conduits for soft waters, but hard waters that have passed through lead pipes may be drunk with impunity.

Lead unites directly with fluorine, chlorine and sulfur. By virtue of its position in the electromotive series of the metals, lead is precipitated from solutions of its salts by zinc, tin and iron. Lead exists in isotopic forms.

Almost all acids react with metallic lead to form the corresponding salts. However, unless the salt which forms is soluble in the acid, it deposits on the surface of the metal and quickly stops further action of the acid on the metal. Sulfuric acid (1) reacts readily with lead to form lead sulfate, but under ordinary conditions the lead sulfate coats the lead, preventing further reaction. This is the reason that lead chambers can be used in the sulfuric acid process (see p. 135). However, from experience it has been found that if the concentration of the sulfuric acid in the lead chambers exceeds 78 per cent, it begins to react with the lead sulfate to form lead bisulfate which is soluble (2). If this happens the lead will be rapidly dissolved.



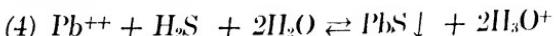
Dilute nitric acid is the best solvent for lead (3), converting the lead to lead nitrate. The concentrated acid is not a desirable solvent because lead nitrate is not very soluble in it.



2. *Lead Ion.*—Lead exists in two states of oxidation, (1) the divalent ( $Pb^{++}$ ) and (2) the tetravalent ( $Pb^{++++}$ ). The former is the more important and is usually spoken of as the "lead ion" or "plumbous ion," the other form being referred to as the "plumbic"

form of lead. We will consider only the chemistry of the plumbous ion.

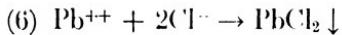
Hydrogen sulfide and soluble sulfides precipitate brownish-black lead sulfide (4) from acid, alkaline or neutral solutions of lead salts. The precipitate is insoluble in dilute acids, in alkali hydroxides, in carbonates, and in sulfides.



Sulfuric acid and soluble sulfates precipitate white lead sulfate (5) from acid or neutral solutions of lead salts. It is insoluble in water and in diluted hydrochloric or nitric acids. The precipitate is completely soluble in warm sodium hydroxide T.S. and in ammonium acetate solution.



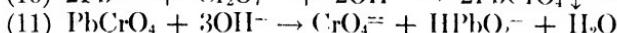
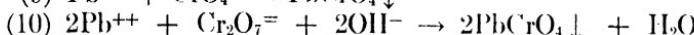
Hydrochloric acid and soluble chlorides precipitate white lead chloride (6) from solutions of lead salts. It is soluble in *hot* water.



Fixed alkalies precipitate white lead hydroxide  $[\text{Pb}(\text{OH})_2]$  from solutions of lead salts (7). The precipitate is soluble in an excess of the precipitant (8).



Chromic acid and soluble chromates ( $\text{K}_2\text{CrO}_4$  and  $\text{K}_2\text{Cr}_2\text{O}_7$ ) precipitate bright yellow lead chromate ( $\text{PbCrO}_4$ ) from solutions of lead salts (9, 10). The solutions should be free or nearly free from mineral acids. The precipitate is insoluble in ammonium hydroxide and in acetic acid but readily dissolves in fixed alkali hydroxides to form *plumbites* (11).

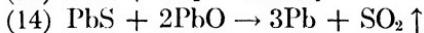
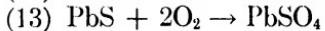
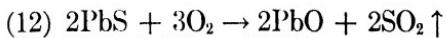


**Official Tests for Identity.**—1. Solutions of lead salts yield a precipitate of lead sulfate with diluted sulfuric acid (5). This precipitate is insoluble in diluted hydrochloric or nitric acids, but is completely soluble in warm sodium hydroxide T.S. or ammonium acetate solution.

2. With potassium chromate T.S., solutions of lead salts will precipitate yellow lead chromate (9, 10) provided the solution is free or nearly free of mineral acids. This precipitate is insoluble in acetic acid, but is soluble in sodium hydroxide T.S. (11).

**Commercial Manufacture.**—Lead is made from galena by roasting the ore at a moderate temperature in a blast furnace. During this initial roasting a part of the lead sulfide is oxidized to oxide (12) and a part to sulfate (13). This ore is then charged with coke and

fluxes in alternate layers to the top of the lead blast furnace which is ordinarily about 35 feet high, 20 feet long, and 10 feet wide, and has 8 or 10 tuyeres along each side. The lead runs out of the furnace through a siphon into a forehearth (14) and (15), while the matte and slag are tapped. The matte contains most of the silver, gold, and copper in the ore, and is subsequently refined. The solidified but impure lead is called "hard lead" and is ready to be purified by various methods.



The *hard lead* is carefully heated until most of the copper, arsenic and antimony are oxidized and removed. The lead still contains silver, gold, and bismuth and, depending upon the amount of silver present, is desilvered in one of three ways.

1. *Pattinson Process*.—This method consists in gradually cooling the molten metals and removing with perforated ladles the pure lead which crystallizes out. By repeated crystallizations, not only is a very pure lead obtained but also a residual metal rich in silver. The latter may be cupellated.

2. *Parkes Process*.—This process is based upon the facts that molten lead and zinc are not miscible in all proportions and that gold and silver are much more soluble in melted zinc than in lead. Therefore, when zinc is added to a molten argentiferous lead, it melts and, having effected the solution of the gold and silver, it rises to the top of the molten mass and may be skimmed off or allowed to solidify. The zinc is then distilled off in retorts, leaving a residue of impure silver. The zinc distillate is used over again to extract silver and gold from molten lead.

3. *Betts Process*.—This is an electrolytic process. A sheet of pure lead (cathode) and a plate of impure lead (anode) are immersed in an electrolyte of lead fluosilicate. When the current is turned on, lead dissolves from the anode and is deposited on the cathode. Any iron that is present goes into solution, whereas, gold and silver remain on the anode. The impure lead is often poled before purifying it electrolytically.

**Pharmacological Action of Lead Ion.**—Aub and his collaborators have shown that lead is stored in the bones, and is mobilized in the circulation by the administration of ammonium chloride, acid sodium phosphate and acid-producing (carbohydrate-free) diets. Administration of potassium iodide also brings the lead into the circulation and, if this occurs too rapidly, toxic phenomena and mania may set in. It is stabilized in the bones by administration of sodium bicarbonate, disodium hydrogen phosphate and alkali-producing diets.

Soluble lead salts precipitate proteins and hence, act as topical astringents. In fact, they are not only the most astringent of all

of the soluble salts of the metals but are also the least destructive of tissue. Lead ion is toxic and, although absorption is rather slow, its action is cumulative and chronic poisoning is produced by continued intakes even of small quantities of lead compounds. Although absorption from intact skin is practically *nil*, lead ion is absorbed in sufficient quantities from denuded or chapped skin to cause lead poisoning.

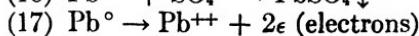
The toxicity of insoluble lead salts depends upon their solubilities in the digestive fluids. In the stomach, insoluble lead salts are converted into lead chloride of which 21.85 millimols dissolve in a liter of 0.2 per cent (0.063 normal) hydrochloric acid. Peptone also facilitates solution of lead salts, probably in protein combination or as lead albuminate.

The inhalation of white-lead dust, fumes from molten lead (consisting chiefly of oxides), atomized spray used in painting, etc., will cause lead poisoning. The symptoms of poisoning appear more quickly when the compounds are inhaled. This is due in part to the fineness of the particles. Absorption takes place from the lungs and nasopharynx and, to a greater degree, from the stomach into which the lead compound is introduced by swallowing the dust. Lead is excreted both in the feces and in the urine.

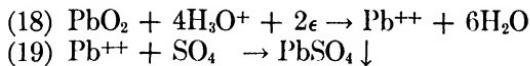
Ten Gm. of the soluble lead salts have produced death and recoveries from 30 Gm. have been reported. The antidotal treatment consists of large doses of magnesium or sodium sulfates (1 or 2 per cent solution) and emptying the stomach. Milk, eggs, and coffee are of value after the stomach is empty. A cathartic should be given to cause rapid elimination of any lead sulfide formed in the bowels.

**Uses.**—Because of its property of resisting the action of air, water and acids, lead is employed for making a large variety of articles, *e. g.*, water pipes, chemical and electrical apparatus, linings for acid-proof vessels (sulfuric acid chambers), valves, insulators for cables, etc. It is also used in making lead salts, lead pigments, white lead, etc. Its use in solders and alloys has been mentioned previously.

Large quantities of lead are used in making *ordinary storage batteries*. The lead accumulator consists of alternate plates of spongy lead and lead dioxide contained in cells which, in turn, are fitted into a wooden or hard rubber case. In a new battery the electrolyte is a diluted sulfuric acid having a specific gravity of 1.275 to 1.290. When the battery is in use, the sulfate ions ( $\text{SO}_4^{=}$ ) migrate toward the spongy lead plates and, by virtue of the *solution pressure* of the lead being greater than the *osmotic pressure* of the ions, the lead goes into solution as lead ions which immediately react with the sulfate ions to form white, sparingly soluble lead sulfate (16), whereas the plates become negatively charged (17).



Simultaneously, the hydronium ions ( $H_3O^+$ ) move toward the plates of lead dioxide where, with the aid of two electrons, tetravalent lead is reduced to the bivalent condition with the formation of water (18). The lead ions, in turn, react with the sulfate ions to form lead sulfate (19).



From the above it will be noted that the electrons flow through the external circuit *from* the lead plates *to* the lead dioxide plates. Furthermore, it will be observed that the chemical reactions in the cell remove both hydronium and sulfate ions from the electrolyte, and hence the potentiality of a cell can be ascertained by taking the specific gravity of the cell fluid.

Just as chemical action within the cell establishes a difference of potential between the lead and lead dioxide plates with an attenuation of the electrolyte, just so may the cell be brought back to its condition before discharge by passing a high voltage current through it in the reverse direction. By this "charging" process, electrical energy is converted into chemical energy, which is evidenced in a fully charged cell by an E.M.F. of about 2 volts.

## OFFICIAL LEAD COMPOUNDS

### LEAD ACETATE

*Lead Acetate*, U. S. P. XIII

Formula,  $Pb(C_2H_3O_2)_2 \cdot 3H_2O$ ;  $(CH_3COO)_2Pb \cdot 3H_2O$

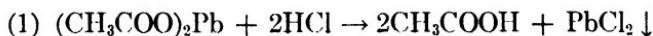
Molecular Weight, 379.35

**Physical Properties.**—Lead Acetate crystallizes with 3 molecules of water in colorless, shining, transparent, monoclinic prisms or plates, or in heavy, white, crystalline masses, or granular crystals. It has a faint odor of acetic acid and a sweet taste, effloresces, and absorbs carbon dioxide from the air. Its density is about 2.55.

One Gm. of lead acetate dissolves in 1.6 cc. of water and in about 30 cc. of alcohol, at  $25^\circ C$ . One Gm. dissolves in 0.5 cc. of boiling water. It is freely soluble in glycerin.

The salt becomes anhydrous when heated at  $40^\circ C$ . At  $75^\circ C$ . it dissolves in its own water of hydration and at temperatures above  $280^\circ C$ . it decomposes into finely divided metallic lead and lead oxide.

**Chemical Properties.**—When acidified, lead acetate is decomposed into acetic acid and the lead salt of the acid, *e. g.*, hydrochloric acid (1). If the acidified solution is warmed, the acetic acid is volatilized to give an odor of "vinegar."



Solutions of lead salts have a strong tendency to precipitate out a white carbonate when in contact with the CO<sub>2</sub> of the air. Although the composition of the carbonate is probably not represented accurately by the formula, PbCO<sub>3</sub>, this will serve to illustrate the precipitation (2).



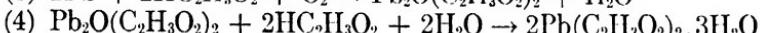
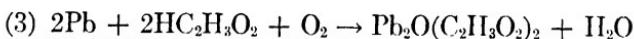
For this reason, it is desirable to use only recently boiled distilled water to dissolve lead acetate, because the boiling process effectively removes dissolved CO<sub>2</sub>.

In all of its other reactions lead acetate exhibits the usual reactions of the plumbous ion (*q. v.*) and of the acetate ion (*q. v.*).

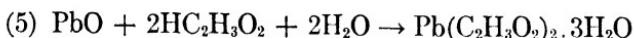
**Official Tests for Identity.**—1. A 1 in 10 solution of the salt responds to the tests for the lead ion (*q. v.*).

2. A solution of lead acetate also responds to the tests for the acetate ion (*q. v.*).

**Commercial Manufacture.**—This salt is made by the action of acetic acid upon metallic lead or litharge. Large quantities of lead acetate are made by allowing concentrated acetic acid to trickle over lead coils or sheets contained in large, open, stone cylinders. During the operation, the lead goes into solution in the form of basic lead acetate (3). In order to obtain the normal salt, the liquid is made slightly acid with acetic acid (4), concentrated and crystallized. Pharmaceutical lead acetate in small granular crystals is prepared by dissolving the large crystals in water, filtering and evaporating the filtrate with constant stirring.



Lead acetate is also made by dissolving litharge (PbO) in acetic acid (5). The resulting solution is made acid with acetic acid, concentrated and crystallized.



**Laboratory Preparation.**—Mix 10 Gm. of litharge, 16 Gm. of Acetic Acid (N. F.), and 8 cc. of distilled water in a porcelain dish, stir well, and allow it to stand for twenty-four hours. At this point the mixture usually becomes a hard mass because acetic acid is lost by evaporation between class periods. A small flask may be substituted for the porcelain dish, which will allow for use of a stopper to prevent the evaporation. Then heat the mixture on a water-bath until the litharge is dissolved. Filter. Evaporate the solution until a pellicle forms, if necessary adding a little more acetic acid to impart a decidedly acid reaction to the solution. Set the liquid aside to cool and crystallize. Collect, drain, and dry the crystals. (See Equation 5 above.)

**Pharmaceutical Preparations and Uses.**—1. *Lead Acetate* (Plumbi Acetas, Sugar of Lead), U. S. P. XIII.—“Lead Acetate contains not less than 85.3 per cent and not more than 89.57 per cent of  $Pb(C_2H_3O_2)_2$ , corresponding to not less than 99.5 per cent of the hydrated salt  $Pb(C_2H_3O_2)_2 \cdot 3H_2O$ .” *Internally*, lead acetate is used very rarely as an astringent in diarrheal and catarrhal inflammations because there is definite danger of acute lead poisoning. *Externally*, lead acetate is used for its astringent properties either as a lotion, or as an injection into the urethra, vagina, etc. The use of lead acetate as a wash in the treatment of poison ivy poisoning is contraindicated. Its use for the treatment of poison ivy was based on the observed fact that lead precipitates the phenolic substances present in poison ivy. However, research has shown that the lead precipitate is just as, if not more, active than the original phenolic substances.

2. *Lead and Opium Lotion* (Lotio Plumbi et Opii, Lead and Opium Wash), N. F. VIII.—This lotion is prepared by dissolving 18 Gm. of lead acetate in 650 cc. of distilled water, adding 35 cc. of opium tincture and finally adding enough distilled water to make 1000 cc. of the finished preparation. A portion of the lead acetate is used up in the precipitation of gums, coloring matter, etc., in the tincture. The balance acts as an astringent. It should be shaken before dispensing. It is used as an external application for sprains and bruises, but is probably of little value because the analgesic effect of morphine (in opium) is not obtained through the skin.

3. *Lead Subacetate Solution* (Liquor Plumbi Subacetatis, Goullard's Extract), N. F. VIII.—This is an aqueous solution containing in each 100 cc., lead subacetate, approximately  $Pb_2O(CH_3COO)_2$ , equivalent to not less than 22.5 Gm. of Pb. It is made by allowing lead monoxide (litharge,  $PbO$ ) to stand for seven days in contact with a solution of lead acetate, or by boiling the mixture of lead acetate, lead monoxide and water for one-half hour, cooling and filtering (6)



A diluted form of lead subacetate solution is official as *Diluted Lead Subacetate Solution* (Liquor Plumbi Subacetatis Dilutus, Lead Water), N. F. VIII. It is prepared by diluting 35 cc. of Lead Subacetate Solution with sufficient recently boiled distilled water to make 1000 cc. of finished product.

Lead Subacetate Solution is also used in preparing *Lead Subacetate Cerate* (Ceratum Plumbi Subacetatis, Goullard's Cerate), N. F. VIII. This cerate consists of 20 per cent of lead subacetate solution incorporated in an ointment base containing wool fat, white wax, white petrolatum and camphor.

The solution and the cerate described above are used for the astringent and antiseptic properties connected with lead subacetate.

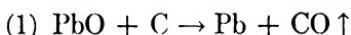
**LEAD MONOXIDE***Lead Monoxide, N. F. VIII*

Formula, PbO. Molecular Weight, 223.21

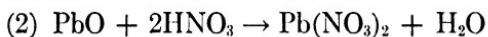
**Physical Properties.**—Lead Monoxide occurs as a heavy, yellowish or reddish powder, or as minute scales, without odor or taste. This variation in color is due to the fact that it occurs in two forms, namely yellow litharge and red massicot. On exposure to air, it slowly absorbs moisture and CO<sub>2</sub>. When it is heated it becomes darker in color but goes back to its original color when cooled again. It fuses at red heat.

The oxide is almost insoluble in water, although it imparts a faintly alkaline reaction to the water. It is insoluble in alcohol but is soluble in acetic acid, diluted nitric acid, and warm solutions of the alkali hydroxides.

**Chemical Properties.**—Lead Monoxide is reduced to free lead when it is heated in contact with charcoal (1).



Its solubility in acids, such as nitric acid (2), is a reaction characteristic of most oxides of metals.



Its solubility in alkali hydroxides is due to the formation of the plumbite ion. Its solubility in sodium hydroxide is characteristic. A stepwise consideration of the reactions involved will serve to better clarify this solubility. The first reaction is undoubtedly the hydration of the oxide to form a small amount of lead hydroxide (3). The lead hydroxide then reacts with sodium hydroxide to form the plumbite (4). As the equilibrium between the unhydrated lead oxide and the hydroxide is disturbed by withdrawing the hydroxide, more of the oxide is hydrated until it is all in solution.



When litharge is mixed with glycerin in the proper proportions, a reaction takes place in which heat is given off and the mixture sets to a hard, cement-like mass. Use is made of this property by plumbers to cement pipe joints together.

**Official Tests for Identity.**—1. A solution of the oxide in diluted nitric acid is colorless and, when nearly neutralized with ammonia T.S., gives the tests for lead ion (*q. v.*).

**Commercial Manufacture.**—Although litharge and massicot are chemically the same (PbO), they are made by different processes.

*Massicot*, in the form of an amorphous yellow powder, is prepared by heating lead hydroxide, carbonate, or nitrate. It is made also by gently heating lead in a reverberatory furnace.

*Litharge*, in the form of a more or less reddish-yellow, scaly, crystalline mass, may be obtained by melting massicot, allowing it to cool slowly and pulverizing. The change in color from that of massicot may be due to the presence of small amounts of red lead ( $Pb_3O_4$ ). A large quantity of litharge is obtained as a by-product in the desilvering of lead ores (*q. v.*). It is made mainly by oxidizing molten lead under specific temperature and oxidizing conditions.

**Pharmaceutical Preparations and Uses.**—1. *Lead Monoxide* (Plumbi Monoxidum, Plumbi Oxidum, Litharge), N. F. VIII.—“Lead Monoxide, when freshly ignited, contains not less than 97 per cent of  $PbO$ .” Lead Monoxide is not used medicinally as such but is used to prepare various other pharmaceutical preparations. It is employed also in metallurgy, ceramics and in making “flint glass,” “driers” for raw linseed oil, varnishes, ceramic cements, paint pigments and rubber.

2. *Lead Oleate Ointment* (Unguentum Plumbi Oleatis, Unguentum Diachylon), N. F. VIII.—This ointment contains 50 per cent of lead oleate plaster incorporated in 49 per cent of white petrolatum by melting the two together. One per cent of lavender oil is added to the mixture when cool. This ointment is used for the antiseptic and astringent effect of lead ion in the treatment of various skin diseases.

3. *Lead Oleate Plaster* (Emplastrum Plumbi Oleatis, Lead Plaster, Diachylon Plaster), N. F. VIII.—Lead Oleate Plaster is made by allowing finely sifted lead monoxide to act upon a mixture of melted lard and olive oil. As soon as lead oleate is formed, it is washed with water to remove glycerin, kneaded until nearly free from water, and the pliable, tenacious mass rolled into cylinders and wrapped in paper. Lead plaster is a mixture of lead oleate, palmitate and stearate. It is used to make Lead Oleate Ointment (*q. v.*).

4. *Lead Subacetate Solution* (Liquor Plumbi Subacetatis, Gouillard's Extract), N. F. VIII.—(See p. 495.)

#### NON-OFFICIAL LEAD COMPOUNDS

**Lead Carbonate.**—Formula  $PbCO_3$  or  $Pb(OH)_2 \cdot 2PbCO_3$ . Lead carbonate ( $PbCO_3$ ) occurs in Nature as the mineral *cerusite*. It may be prepared by pouring a solution of ammonium carbonate into a solution of lead acetate. When washed and dried, the precipitate is a white crystalline solid.

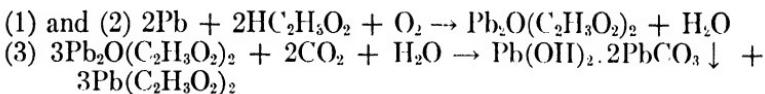
While several *basic carbonates of lead* are known, their composition is still in doubt. The best known basic lead carbonate is *white lead* (ceruse, flake lead). It is used extensively as a paint pigment. The formula  $Pb(OH)_2 \cdot 2PbCO_3$  has been assigned to it.

Nearly all of the processes for making basic lead carbonates depend upon the conversion of metallic lead into acetate with the subsequent conversion of the latter into basic carbonate by the action of carbon dioxide.

The processes used for making white lead are all based upon the

general method just given and differ only as to application and the source of carbon dioxide. The *Dutch process* or *corrosion process* is by far the oldest one and is used in Holland, Belgium, Germany and the United States. Sheets of lead are rolled into scrolls or cast into "buckles" and placed on projections, in earthenware pots or jars. A small quantity (about 250 cc.) of 2.5 per cent acetic acid is poured into the jars in such a manner as not to come in direct contact with the lead. The jars are covered with overlapping boards and arranged together in layers or "tiers." They are then surrounded and covered with spent tan bark which, when it ferments, generates sufficient heat to vaporize some of the acetic acid. This, in turn "corrodes" the lead with the formation of a basic lead acetate, which then is slowly acted upon by the carbon dioxide from the fermenting tan bark to form basic lead carbonate or white lead. After some weeks the basic lead carbonate is removed or "stripped" from the stack of pots.

A more rapid method in quite general use is the *Carter process*, sometimes called the *quick process*. Molten lead is passed in front of a high-pressure steam jet. The steam atomizes the lead and partially oxidizes it. This finely divided lead is placed in two large revolving wooden drums provided with a trunnion, where it tumbles over dilute acetic acid (about 2 per cent). Carbon dioxide, obtained by carefully regulating the oxidation of coke, is passed in at one end of the drum and out the other. The lead acetate that is first formed (1) is converted by air into basic lead acetate (2). This is acted upon by carbon dioxide and forms basic lead carbonate (3) and normal lead acetate. The latter is again changed to basic acetate, and so on, until all of the lead has been converted into basic carbonate.



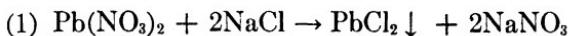
The process usually takes about fifteen days.

The white lead is ground moist (to keep down dust) in plate-mills and then screened. Next, the material is "floated," the lighter particles being allowed to settle while the heavier ones are returned to the mill. When the moist white lead obtained from the settling vats is mixed with boiled linseed oil, the latter displaces practically all (more than 99.5 per cent) of the water and forms what is commonly known as *white lead paste*.

White lead is sometimes used in the form of a 10 per cent ointment against dermatitis, burns, etc. It is employed chiefly in the manufacture of paints.

**Lead Chloride.**—Formula  $\text{PbCl}_2$ , Molecular Weight, 278.12. Lead chloride is found in Nature as the mineral *cotunnite*. It may be prepared by the action of chlorine upon lead or by treating the oxide with hydrochloric acid. Soluble chlorides precipitate lead chloride from solutions of lead salts (1). It is soluble in about

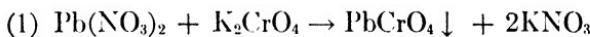
95 parts of water at 25° C. and in 30 parts of boiling water. It crystallizes from cooled solutions in the form of white, needle-shaped, rhombic crystals. These crystals melt at 498° C.



It was used as a sedative and astringent in the form of a dusting powder or, as an ointment, for burns and inflamed skin.

When litharge and ammonium chloride are heated together, an oxychloride, known as *Cassel's yellow* or *Turner's patent yellow*, is formed. It is used as a pigment.

**Lead Chromate.**—Formula  $\text{PbCrO}_4$ , Molecular Weight, 323.22. Lead chromate (Chrome-, Leipzig-, Paris-, Cologne-, King's-yellow). A bright lemon-yellow precipitate of lead chromate is formed when a solution of a lead salt is treated with a soluble chromate or dichromate (1).



It has a density of about 6.123 and decomposes at 600° C. It dissolves in strong alkalies to form plumbites (2).

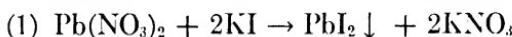


When boiled with a dilute alkali, it forms a basic salt ( $\text{PbCrO}_4 \cdot \text{PbO}$ ) known as *chrome red*.

**Lead Iodide.**—Formula,  $\text{PbI}_2$ , Molecular Weight, 461.05. Lead iodide occurs as heavy, golden yellow, laminar crystals or as a powder. It is odorless and tasteless, has a density of 6.16 and melts at 402° C. It is stable in air.

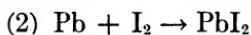
One Gm. is soluble in about 1300 cc. of water at 25° C. and in about 200 cc. of boiling water. It is sparingly soluble in alcohol. It readily dissolves in solutions of fixed alkalies and in concentrated solutions of potassium iodide, alkali acetates, and sodium thiosulfate. Lead iodide dissolves also in a hot solution of ammonium chloride.

Lead iodide is made by adding an aqueous solution of lead nitrate to an aqueous solution of potassium iodide (1).



The precipitate is washed with cold water and then dissolved in the minimum amount of boiling water, from which it is allowed to crystallize.

A recent patent<sup>1</sup> for the manufacture of lead iodide makes use of the reaction between molten lead and iodine. Iodine vapor, diluted with helium or nitrogen to control the reaction, is passed through molten lead (2).

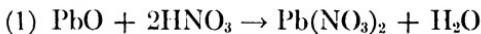


Lead iodide was recognized under the title *Plumbi Iodidum* by N. F. V. It is infrequently used in the form of an ointment as

<sup>1</sup> U. S. patent, No. 2,366,953.

a mild counterirritant against glandular swellings, etc. A technical grade of the salt is used in bronzing, mosaic gold, in printing and in photography.

**Lead Nitrate.**—Formula  $\text{Pb}(\text{NO}_3)_2$ , Molecular Weight, 331.23. Lead nitrate is made by dissolving metallic lead or lead monoxide in nitric acid (1).



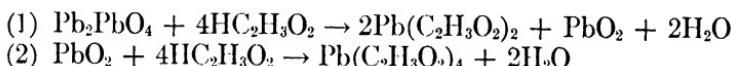
It crystallizes in large, anhydrous, regular or monoclinic crystals, isomorphous with barium nitrate. The salt is soluble in 1.85 parts of water at  $25^\circ\text{C}$ . and in less than its own weight (0.75 cc.) of boiling water. It is nearly insoluble in alcohol. When heated to about  $470^\circ\text{C}$ ., it decomposes into nitrogen dioxide, oxygen and litharge (2).



Because of its high density (4.53), lead nitrate is advantageously used in place of ammonium or sodium nitrate for making match heads and commercial and military explosives. It is used also in the dyeing industry.

**Red Lead Oxide** (Red Lead, Minium, Lead Orthoplumbate).—Formula  $\text{Pb}_2\text{PbO}_4$ , Molecular Weight, 685.63. Red lead is a heavy, odorless and tasteless, orange-red powder having a density of 8.6 to 9.1. It slowly absorbs carbon dioxide and moisture from the air.

Red lead oxide is nearly insoluble in water and is insoluble in alcohol. It is dissolved by an excess of glacial acetic acid (1) (2) to form unstable plumbic acetate. It is dissolved also by lactic acid with the evolution of carbon dioxide and the odor of acetaldehyde.



When red lead oxide is heated in a porcelain crucible, it becomes dark red, then violet, and finally almost black. On cooling, it assumes its original color. Prolonged exposure to high temperatures decomposes it into lead monoxide and oxygen.

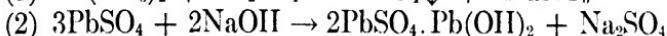
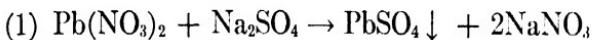
When heated with charcoal, it is reduced to metallic lead.

Red lead or minium is made by heating litharge to about  $450^\circ\text{C}$ . in a reverberatory or muffle furnace. It is made also by heating a mixture of litharge and either sodium nitrate or potassium chlorate to a dark red heat.

Formerly recognized by the N. F. V. under the title of *Plumbi Oxidum Rubrum* (Red Lead Oxide), it was required to contain lead orthoplumbate ( $\text{Pb}_2\text{PbO}_4$ ) usually with some unconverted lead monoxide ( $\text{PbO}$ ), corresponding to not less than 30 per cent of lead dioxide ( $\text{PbO}_2$ ). Red lead oxide is used in ceramics, ceramic cements, matches, red pencils, etc. When employed as a pigment in paints for use on iron and steel, it seems to retard corrosion.

**Lead Sulfate.**—Formula  $\text{PbSO}_4$ , Molecular Weight, 303.27. Native lead sulfate occurs as transparent rhombic or monoclinic

crystals in the mineral *anglesite*. The crystals of lead, strontium, and barium sulfates are isomorphous. It is made by adding a soluble sulfate to a solution of a lead salt (1). The product is a heavy, white, crystalline solid, which is difficultly soluble in water and dilute acids. Concentrated sulfuric or nitric acids will dissolve it. It is also soluble in solutions of ammonium acetate, sodium thiosulfate, and fixed alkalies (2).



Both lead sulfate and basic lead sulfate are used as paint pigments. Basic lead sulfate is sometimes called *sublimed white lead*.

## THE PHOSPHORUS FAMILY

**Introduction.**—*Nitrogen* and *phosphorus* are the short-period elements that belong to this group. The members of Division A are *arsenic* (As, at. wt. 74.91), *antimony* (Sb, at. wt. 121.76) and *bismuth* (Bi, at. wt. 209). These five elements constitute what is known as the *phosphorus family*, and vary in their physical and chemical properties in the order of the atomic weights. Following nitrogen, which is the representative member of the family, each element forms a transition link in the chain of properties between the one immediately preceding and the one immediately following it.

The following are some of the more important similarities and dissimilarities in physical and chemical properties that exist between the various members of this group: There is a wide difference between the properties of the first and last member of this family. For example, nitrogen is non-metallic, whereas bismuth is almost entirely metallic. Nitrogen forms active acids, whereas bismuth is considered as being a base-forming element. Nitrogen has a variable valence, but bismuth is usually trivalent.

Nitrogen and phosphorus show no marked similarities other than being non-metals which possess the same normal family valence of 3. Their respective compounds do not exhibit any striking resemblances. These elements differ greatly in many respects. For example, the combination of nitrogen with oxygen takes place only at high temperatures and the union is endothermal ( $\text{N}_2 + \text{O}_2 + 43,000 \text{ cal.} \rightleftharpoons 2\text{NO}$ ). On the other hand, phosphorus spontaneously unites with the oxygen of the air and burns with the evolution of a large quantity of heat. Nitric acid ( $\text{HNO}_3$ ) is unstable and is a powerful oxidizing agent, whereas the corresponding acid of phosphorus, metaphosphoric acid ( $\text{HPO}_3$ ) is stable and is not an oxidizing agent. Nitrogen unites directly with hydrogen; phosphorus, arsenic and antimony combine indirectly with it; and bismuth does not form a hydride. Only one of these hydrides ( $\text{NH}_3$ ) unites with water to form a base. Nitrogen and phosphorus by themselves do not form positive ions. Trivalent arsenic gives a positive ion ( $\text{As}^{+++} + 3\text{Cl}^-$ ), but does not form normal salts such as the sulfate or nitrate. Both antimony and bismuth give positive trivalent ions and form normal salts which are rather easily hydrolyzed to the hydroxide or to basic salts.

Nitrogen, phosphorus and arsenic are non-metals and mainly acid-forming. The transition to base-forming metallic bismuth is effected through antimony which, when *pentavalent*, is non-metallic and therefore acid-forming ( $\text{HSbO}_3$ ), but when *trivalent* [ $\text{Sb}_2(\text{SO}_4)_3$ ] is base-forming and thus acts like a metal. Arsenic, antimony and bismuth do not displace hydrogen from dilute acids.

The elements of Division B, Group V are *vanadium* (V, at. wt. 50.95), *columbium* (Cb, at. wt. 92.91) and *tantalum* (Ta, at. wt.

180.88). Their valences vary considerably. For example, vanadium exhibits valences from 1 to 5 inclusive, columbium from 2 to 5 inclusive, and tantalum forms compounds in which it shows valences of 2, 4 and 5. These elements normally act as metals, but sometimes, especially in their higher valences, they possess non-metallic properties. The properties of analogous compounds of these elements are very similar. Vanadium (atomic number, 23) has many physical and chemical properties in common with chromium (atomic number, 24) and manganese (atomic number, 25). Columbium (atomic number, 41) resembles molybdenum (atomic number, 42), and tantalum (atomic number, 73) has many similar properties to tungsten (atomic number, 74).

## CHAPTER XXXV

### PHOSPHORUS AND PHOSPHORUS COMPOUNDS

#### PHOSPHORUS

Symbol, P. Valence, III, V. Atomic Weight, 30.98;  
Atomic Number, 15

**History.**—The name phosphorus (Greek, φως, light, φέρω, I bear) was given originally to all phosphorescent substances, *i. e.*, those having the power of shining in the dark, but now its use is restricted to a non-metallic element which was first known as "phosphorus mirabilis" or "phosphorus igneus." This element was obtained in 1669 by Brand, a Hamburg alchemist, by evaporating urine to dryness and distilling the residue with sand. Kraft bought the secret of its preparation from its originator and in 1677 exhibited specimens of phosphorus in England, where it caused great excitement among chemists. Working independently, Kunckel, in 1678, and Boyle, in 1680, succeeded in obtaining the element. In 1769, Gahn showed that bones were composed largely of calcium phosphate, and in 1771 Scheele prepared phosphorus by treating bone ash with nitric acid, precipitating the calcium as calcium sulfate, filtering, evaporating and distilling the residue with charcoal. Later, the Scheele process was improved by Nicolas and Pelletier, who decomposed the bone ash directly with sulfuric acid.

**Occurrence.**—This element is never found as such in Nature, but occurs in combination as native *calcium phosphate* (generally known as *phosphorite* or "phosphate rock") in large deposits in Georgia, Florida, Tennessee, Utah, Idaho, Montana, Wyoming, Alabama, the Carolinas and Algeria. A mineral known as *apatite*,  $\text{Ca}_3(\text{PO}_4)_2 \cdot \text{CaF}_2$ , is found in large quantities in Canada. Phosphorus is essential to animal and vegetable life. It occurs in bones and teeth (58 per cent calcium phosphate), blood, urine and in considerable quantities in the nervous, muscle and brain tissue as complex organic compounds called *phosphoproteins*.

**Physical Properties.**—Commercial phosphorus may be obtained in two forms, *viz.*, white phosphorus and red phosphorus.

**White Phosphorus.**—White phosphorus, as usually prepared, is a pale yellow, transparent, waxy solid, having a density of 1.82, melting at 44.3° C., and boiling at 280° C. It is thought that the yellow color of phosphorus is occasioned by the presence of small quantities of red phosphorus. The pure white element may be obtained by heating the yellow phosphorus with chromic acid solution, washing, and drying it in a vacuum, first at 40° C. and then at 80° C. The element will remain colorless if kept in vacuum tubes in the dark, but upon exposure to light it rapidly turns yellow. The fracture of phosphorus is distinctly crystalline; large, regular, duodecahedral or octahedral lustrous crystals being obtained by crystallization from carbon disulfide or by sublimation in the absence of air.

Phosphorus is nearly insoluble in water. At 25° C., 1 Gm. of phosphorus dissolves in 0.9 cc. of carbon disulfide, about 400 cc. of anhydrous alcohol, about 40 cc. of chloroform, 102 cc. of anhydrous ether, 31.5 cc. of benzene, in sulfur chloride, and it is sparingly soluble in fixed oils and oil of turpentine. *It is very poisonous*, 0.15 Gm. being the lethal dose. Exposure to phosphorus vapors produces necrosis. It is a non-conductor of electricity. Molten phosphorus boils at 280° C. and forms colorless vapors which at approximately the boiling-point, correspond in density to a tetraatomic molecule, P<sub>4</sub>. Blitz and Meyer, working at higher temperatures (1500° to 1700° C.), found dissociation into P<sub>2</sub> molecules. Beckmann obtained P<sub>4</sub> molecules from the boiling-points of carbon disulfide solutions, and Hertz arrived at the same conclusion from the lowering of the freezing-point in benzene solution.

**Red Phosphorus.**—Red phosphorus occurs as a dark purplish-red to violet, microcrystalline, non-poisonous (when pure) powder which is insoluble in all solvents. Its density varies from 2.05 to 2.34. The variability of its heat of combustion, together with its other non-constant physical properties, preclude its being considered as a simple allotropic form of phosphorus. It is thought to be a more or less pure *solid solution* of scarlet phosphorus in metallic or black phosphorus. It is stable in air and light. Under a pressure of 43 atmospheres, it melts at 590° C. It crystallizes in the regular system. On account of its stability and its non-poisonous property, it is produced in large quantities for consumption in the match industry.

**Allotropic Modifications of Phosphorus.**—A number of modifications of phosphorus are said to exist. Besides ordinary *white phosphorus* there seems to be three rather well-defined forms, all of which are claimed to be true allotropic modifications. In 1905, R. Schenck obtained a *scarlet amorphous powder* by boiling a solution of white phosphorus in either phosphorus tribromide or tri-iodide, or in the sulfide. The powder may be obtained also by heating phosphorus tribromide with mercury at 240° C. This *scarlet phosphorus* is

non-poisonous. When heated, it is converted into red phosphorus. When mixed with potassium chlorate, it is used in the match industry. *Violet phosphorus* is obtained by heating white phosphorus with a minute quantity of sodium to 200° C. under very high pressure. Hittorf prepared *metallic* or *black phosphorus* by heating phosphorus with lead in a sealed tube at 530° C., and recovering the lead by boiling the product with nitric or hydrochloric acid. It occurs as minute, lustrous, black, rhombohedral crystals.

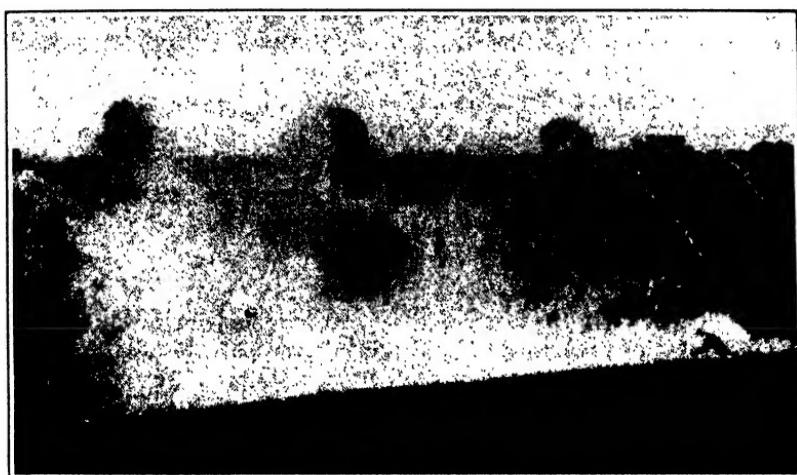


FIG. 19.—White phosphorus shell, 75 mm. two minutes after bursting. (From Fries and West, Chemical Warfare, courtesy of McGraw-Hill Company.)

**Chemical Properties.**—*White phosphorus* combines directly with most of the elements, and hence is a very chemically active substance. Moistened phosphorus is slowly oxidized in air to ozone, phosphorous and phosphoric acids. It is oxidized so rapidly in air that it takes fire at about 35° C. and burns with a bright, white flame to form dense, snow-white clouds of phosphorus pentoxide. Shells and hand grenades containing white phosphorus (W. P.) have been used for incendiary and screening purposes (Fig. 19). It is also easily oxidized by oxidizing agents, *e. g.*, nitric acid (1) to form phosphoric acid and nitric oxide.



When phosphorus or solutions of it in some essential oils, chloroform, etc., are exposed to the air, the element undergoes slow combustion which is revealed by a greenish-white phosphorescence when viewed in the dark. The glowing is always accompanied by the evolution of hydrogen dioxide and ozone (garlic-like odor). Many theories have been advanced to explain this action, but recent investigations lend support to the views that it is due either to the combustion of an oxide more volatile than phosphorus or, that the chemical

energy transformed in connection with the oxidation of the phosphorus is partly converted into radiant energy instead of heat.

*Red Phosphorus.*—The equation (7) representing the reaction that takes place in the manufacture of red phosphorus from white phosphorus clearly shows that the former contains much less internal energy than the latter, and hence is less active chemically. Only when heated to 240° C. or above does red phosphorus unite with the oxygen of the air and ignite.

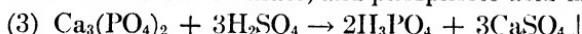
**Tests for Identity.**—1. By its phosphorescence.

2. When white phosphorus is placed in a flask from which the air has been displaced by coal gas (to prevent an explosion), a 30 per cent sodium hydroxide solution run in through a dropping funnel, and the mixture heated, phosphine is evolved and sodium hypophosphite is formed (2). The phosphine made in this way contains a trace of the spontaneously inflammable (liquid) dihydrogen phosphide ( $P_2H_4$ ). If the gaseous mixture is passed through water, the bubbles, upon coming in contact with the air, are immediately oxidized to phosphorus pentoxide (white smoke) and a mist of phosphoric acid.

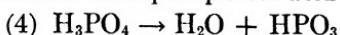


3. When phosphorus is treated with nitric acid, orthophosphoric acid and NO are produced (1). The former may be identified by appropriate tests for phosphate ion.

**Commercial Manufacture.**—*White Phosphorus.*—Formerly, all of the phosphorus of commerce was made from bone-ash, but now the less expensive calcium phosphate (phosphorite) of fossil origin is used. Bone-ash or calcium phosphate is treated with sulfuric acid (specific gravity, 1.5 to 1.6), heated with steam and stirred in a wooden vat. During the heating, the larger part of the calcium is converted into calcium sulfate, and phosphoric acid is obtained (3).



The mixture is filtered and the weak phosphoric acid solution concentrated in leaden pans. During the concentration most of the remaining calcium sulfate is deposited. The syrupy crude phosphoric acid is then mixed with charcoal, coke or sawdust and dried in a muffle furnace. Stourbridge clay retorts, arranged in a galley furnace, are then heated to a bright red heat and charged with the mixture. At red heat, the phosphoric acid loses water and is converted into metaphosphoric acid (4).



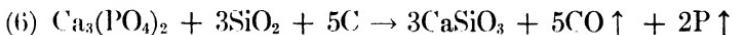
As the temperature of the retorts is gradually raised to a white heat, the metaphosphoric acid is reduced by the carbon to phosphorus which distils (5). The vapors are led through malleable iron pipes into condensing troughs containing cold water.



Most phosphorus is now made by continuously charging a mixture of calcium phosphate, silica (sand) and coke into an electric furnace<sup>1</sup>

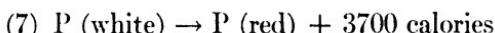
<sup>1</sup> See also, Phosphoric Acid, p. 125.

provided with a close-fitting cover having an outlet leading to a condenser. The discharging of an alternating current between carbon electrodes produces a very high temperature. At the temperature of the furnace the silica attacks the calcium phosphate and forms calcium silicate ( $\text{CaSiO}_3$ ) and phosphorus pentoxide ( $\text{P}_2\text{O}_5$ ). (See p. 129.) The latter is reduced by the carbon to carbon monoxide and phosphorus, which pass over to the condensers (6).



The impure phosphorus,<sup>1</sup> obtained by either process, is purified by melting under water and filtering, first, through animal black and then, through chamois skin. The molten phosphorus is sometimes purified by washing with a weak solution of potassium dichromate and sulfuric acid. By this treatment, the impurities rise to the surface as a scum and may be removed. At one time, workmen sucked up the molten phosphorus in glass tubes in which it was allowed to solidify. On account of the danger to the health of the operators, this method of casting has been replaced by a continuous process, whereby the molten phosphorus is drawn off by suction into cooled tin tubes, where it solidifies as a continuous rod.

*Red Phosphorus.*—Red phosphorus is made by heating white phosphorus at a temperature of  $230^{\circ}\text{ C.}$  to  $300^{\circ}\text{ C.}$  for twenty-four hours in an iron pot fitted with an air-tight lid which is provided with a long pipe of small diameter open to the air (7). At the beginning of the operation, a small quantity of the phosphorus combines with the oxygen of the air present in the vessel to form the pentoxide. The heating is then continued in an atmosphere of inert nitrogen. When the change is complete, the product is ground under water, boiled with caustic soda to free it from any unchanged white phosphorus, washed, dried and packed in tin boxes.



**Pharmaceutical Preparations and Uses.**—Phosphorus and its preparations (Elixirs, and Phosphorated Oil), official in N. F. VII, were deleted from the N. F. VIII. This was no doubt due to the fact that its therapeutic value is very questionable. It was defined as a yellow allotropic form of phosphorus (P). When taken internally in small doses ( $\frac{1}{100}$  grain) the only noticeable effects are an increased formation of bony and connective tissue. It is supposed to exert a gentle stimulating action upon the nervous system. It is used in cases of nervous exhaustion, sexual impotency, rickets and in other disorders of the nervous and bony systems characterized by poor development. *In large doses it is a lethal poison.* A solution of copper sulfate (0.5 Gm. [ $7\frac{1}{2}$  grains]  $\text{CuSO}_4$  in 120 cc. of  $\text{H}_2\text{O}$ ) is the best antidote for phosphorus poisoning. Any free particles or

<sup>1</sup> The Monsanto Chemical Company announces that by an improved electro-thermal process they are able to reduce phosphate rock and subsequently condense elemental phosphorus of better than 99.9 per cent purity.

globules of free phosphorus are coated with a layer of metallic copper. On account of the formation of turpentine-phosphoric acid, old turpentine or French oil of turpentine is said to be an effective antidote. Average dose—Metric, 0.6 mg.; Apothecaries,  $\frac{1}{100}$  grain.

Aside from its medicinal uses, phosphorus has been used in rat poisons, which have been named "Electric Rat Paste," etc., because of their phosphorescence.

### PHOSPHORUS COMPOUNDS

**Phosphides and Phosphines.**—Phosphorus combines directly with the halogens, sulfur, selenium and, in fact, with almost all of the elements to form phosphides. Most of the metals burn in phosphorus vapor. Some metallic phosphides may be made by reducing the phosphates with carbon.

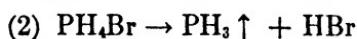
Phosphorus forms three hydrides, *viz.*, phosphine ( $\text{PH}_3$ ), dihydrogen phosphide ( $\text{P}_2\text{H}_4$ ), and solid hydrogen phosphide ( $\text{P}_{12}\text{H}_6$ ). Collectively, they are known as the *phosphines*. The putrefaction of organic material containing phosphorus gives rise to the phosphines, which, upon slow bacterial oxidation, are thought to cause the light of phosphorescence known as the *will-o'-wisp* or *ignis fatuus*, sometimes observed at night over marshy ground, around tree stumps, etc.

Phosphine was first obtained by Gengembre, in 1789, by the action of potassium hydroxide upon phosphorus. This gas was spontaneously inflammable and was thought to be distinct from a non-spontaneously inflammable phosphine which Sir H. Davy obtained some time later by heating phosphorous acid. In 1835, Le Verrier proved that the spontaneous inflammability of Gengembre's phosphine was caused by small quantities of dihydrogen phosphide.

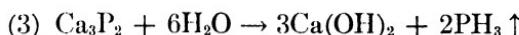
Phosphine ( $\text{PH}_3$ ) is a colorless, poisonous gas with an odor of rotten fish. Unlike the corresponding nitrogen hydride ( $\text{NH}_3$ ), it is only sparingly soluble in water and does not form a basic compound analogous to ammonium hydroxide. It liquefies at  $-90^\circ \text{ C}$ . and becomes a solid at  $-132.5^\circ \text{ C}$ . It is soluble in a solution of copper sulfate and in an acidulated solution of cuprous chloride. Phosphine is easily decomposed by heat into its constituent elements. It inflames spontaneously at  $100^\circ \text{ C}$ . A mixture of phosphine and oxygen is explosive. The halogens violently decompose phosphine. The hydrogen halides unite with it to form a series of phosphonium salts (1).



These compounds are analogous to the ammonium salts of the hydrohalogen acids. They differ from the ammonium salts, however, by not ionizing in aqueous solution. Instead, they decompose into phosphine and the respective halogen acid (2).



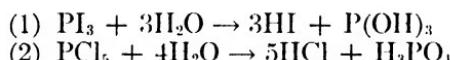
Impure phosphine may be made by the method described on p. 506. Hydrogen and dihydrogen phosphide are also formed during the reaction and contaminate the phosphine. A dihydrogen phosphide-free gas may be obtained by passing the gas obtained in the manner described, into a hydrochloric acid solution of cuprous chloride. This dissolves the  $\text{PH}_3$ , but permits the  $\text{P}_2\text{H}_4$  to pass on. Phosphine, free from  $\text{P}_2\text{H}_4$ , may be obtained by heating this solution. It may be obtained also by the hydrolysis of metallic phosphides (3).



**Dihydrogen Phosphide ( $\text{P}_2\text{H}_4$ ).**—Dihydrogen phosphide was obtained by P. Thenard about 1844. It is a colorless liquid which boils between  $57^\circ$  and  $58^\circ$  C. It is insoluble in water, but dissolves in alcohol and in ether. It is very unstable to heat and light. It may be obtained by decomposing calcium phosphide with warm water and passing the evolved gases through a U-tube contained in a freezing mixture.<sup>1</sup>

**Solid Hydrogen Phosphide.**—The hydride,  $\text{P}_{12}\text{H}_6$ , is an odorless, canary-yellow, amorphous solid. It is obtained by passing the gases resulting from the decomposition of calcium phosphide with warm water, over granular calcium chloride.

**Halides of Phosphorus.**—Phosphorus unites directly with the halogens to form the respective tri- and pentahalides. These halides are hydrolyzed by water to the respective hydrogen halide and phosphorous and phosphoric acids (1) (2).



Below are listed the phosphorus halides with their properties:

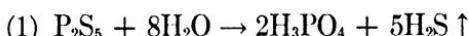
A MODIFICATION OF TABLE IN GENERAL INORGANIC CHEMISTRY  
(SNEED AND MAYNARD)

Compound	Physical state	Color	Heat of formation in calories	M. P.	B.P.	Discoverer
Trifluoride ( $\text{PF}_3$ )	Gas	Colorless	108,000	-160°	-95 0°	Davy
Pentafluoride ( $\text{PF}_5$ )	Gas	Colorless	...	-93 7°	-84 5°	Thorpe
Trichloride ( $\text{PCl}_3$ )	Liquid	Colorless	76,940	-91°	76°	Gay-Lussac, Thenard
Pentachloride ( $\text{PCl}_5$ )	Solid	Yellow-white	106,600	166 8°	162 0°	Davy
Tribromide ( $\text{PBr}_3$ )	Liquid	Colorless	45,400	-40°	Sublimes at 172 9°	
Pentabromide ( $\text{PBr}_5$ )	Solid	Orange-yellow	60,690	*	*	
Tri-iodide ( $\text{PI}_3$ )	Solid	Orange-red	11,000	61°	*	
Tetra-iodide ( $\text{P}_2\text{I}_4$ )	Solid	Orange	19 800	124 5°	*	

\* Decomposes.

<sup>1</sup> Compt. rend. Soc. de biol. de Paris, **18**, 652 (1844); Ber., **23**, 1174 (1890).

**Sulfides of Phosphorus.**—Sulfur and phosphorus energetically combine to form three known sulfides, *viz.*,  $P_2S_5$ ,  $P_4S_7$  and  $P_4S_3$ . When a mixture of red phosphorus and sulfur is heated, the union takes place quietly.  $P_2S_5$  is a yellow powder resembling flowers of sulfur in appearance. It melts at about  $276^{\circ}\text{ C}$ . Tetraphosphorus heptasulfide ( $P_4S_7$ ) occurs in small, faintly yellow prisms which melt at  $310^{\circ}\text{ C}$ . and boil at  $523^{\circ}\text{ C}$ . Tetraphosphorus trisulfide ( $P_4S_3$ ) occurs as light yellow crystals that melt at  $172.5^{\circ}\text{ C}$ . It is used in the match industry. The pentasulfide is readily hydrolyzed by water to orthophosphoric acid and hydrogen sulfide (1).



These sulfides are used in the manufacture of organic compounds and matches.

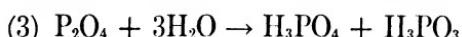
**Oxides of Phosphorus.**—Phosphorus forms three well-defined oxides, *viz.*, phosphorus pentoxide ( $P_2O_5$ ), phosphorus tetroxide ( $P_2O_4$ ), and phosphorus trioxide ( $P_2O_3$ ).

**Phosphorus Pentoxide** ( $P_2O_5$ ).—This soft, flocculent powder is formed by the complete oxidation of phosphorus in the absence of moisture. In 1740, Marggraf named this compound “flowers of phosphorus.” It is very stable in dry air. It has a specific gravity of 2.387 ( $\frac{29}{4}^{\circ}\text{ C}$ .) and melts at approximately  $563^{\circ}\text{ C}$ . With water, a vigorous exothermic reaction takes place to form metaphosphoric acid (1), which is rapidly changed to orthophosphoric acid if the water is warm and in excess (2).



Because of its great affinity for water, it is used for drying gases.

**Phosphorus Tetroxide** ( $P_2O_4$ ).—Phosphorus tetroxide, together with some red phosphorus, is formed when phosphorus trioxide is heated between  $210^{\circ}\text{ C}$ . and  $290^{\circ}\text{ C}$ . It combines with water to form a mixture of phosphorus and phosphoric acids (3).



**Phosphorus Trioxide** ( $P_2O_3$ ).—Phosphorus trioxide was discovered by Sage in 1777. It is formed when phosphorus is burned with a limited amount of oxygen. It is a white powder that melts at about  $22.5^{\circ}\text{ C}$ . It has a specific gravity of 2.135 ( $\frac{29}{4}^{\circ}\text{ C}$ .). Like the other oxides of phosphorus, it acts upon water to form acids. With *cold* water, it slowly reacts to form phosphorous acid; but with *hot* water, it is violently decomposed into red phosphorus, phosphine, dihydrogen phosphide and phosphoric acid.

**Acids of Phosphorus.**—See Inorganic Acids.

## CHAPTER XXXVI

### ARSENIC AND ARSENIC COMPOUNDS

#### ARSENIC

Symbol, As. Valence, III, IV, V. Atomic Weight 74.91;  
Atomic Number, 33

**History.**—This non-metallic element was known to the ancients in the form of its native sulfides, *realgar* and *orpiment*. Aristotle (384–322 B.C.) called these sulfides *sandarace*. Later, Theophrastus (372–287 B.C.) gave them the name, *arsenicon*. The Greek alchemist, Olympiodorus, made *white arsenic* ( $\text{As}_2\text{O}_3$ ) by roasting the sulfides of arsenic. This compound was known to Geber and the later alchemists. About 1250, Albertus Magnus obtained the free element as did Schröder in 1694. In 1733 G. Brandt showed that white arsenic was an oxide of this element which he was possibly the first to obtain in pure form.

**Occurrence.**—Uncombined arsenic is found in Nature in the form of gray colored masses or acicular crystals (rare). In combination, arsenic is widely distributed. Its principal minerals are *realgar* ( $\text{As}_2\text{S}_2$ ), *orpiment* ( $\text{As}_2\text{S}_3$ ), *tennantite* ( $\text{As}_2\text{S}_3 \cdot 4\text{Cu}_2\text{S}$ ), *enargite* ( $\text{Cu}_5\text{AsS}_4$ ) and *arsenopyrite* or *mispickel* ( $\text{FeAsS}$ ). *Cobalt glance* ( $\text{CoAsS}$ ) and *nickel glance* ( $\text{NiAsS}$ ) also contain arsenic in combination. Copper and gold ores are usually associated with one or more arsenic minerals. Traces of arsenic-bearing minerals are found in nearly all naturally occurring metallic sulfides, especially zinc and iron.

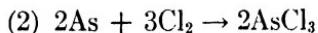
**Physical Properties.**—Arsenic is a steel-gray, brittle solid having a distinct metallic luster. It crystallizes in rhombohedrons, has a density of 5.63 to 5.73 and is a good conductor of electricity. It is insoluble in water. Arsenic sublimes at about  $450^\circ\text{ C}$ . (760 mm.) without melting, the vapors having a yellow color and a garlic-like odor. Fusion takes place only when the element is heated under a pressure of 36 atmospheres. It then melts at approximately  $817^\circ\text{ C}$ . At  $644^\circ\text{ C}$ ., the vapors have a density that corresponds to a formula  $\text{As}_4$ , but at  $1700^\circ\text{ C}$ . the vapor density drops considerably in value due to the dissociation of the  $\text{As}_4$ , and then corresponds to  $\text{As}_2$ . Arsenic resembles phosphorus by existing in one or more allotrophic modifications. There are two well-known forms. When arsenic is sublimed in a current of hydrogen or when arsine ( $\text{AsH}_3$ ) is heated, a black *amorphous* form of arsenic is deposited. When the yellow vapors of arsenic are condensed, a grayish-white *crystalline* form of arsenic is obtained. The amorphous variety of arsenic may be converted to the crystalline form by heating it to about  $360^\circ\text{ C}$ .

**Chemical Properties.**—The chemical properties of arsenic and its compounds present a somewhat complex picture. They will be discussed as (1) elemental arsenic, (2) trivalent arsenic, and (3) pentavalent arsenic.

1. *Arsenic* is permanent in dry air but tarnishes in moist air. It ignites at about 180° C., burns with a bluish flame and evolves white clouds of arsenic trioxide (1).



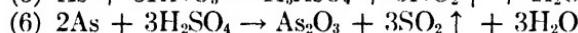
In an atmosphere of chlorine or bromine, arsenic catches fire and forms the trichloride (2) or tribromide, as the case may be.



However, the presence of water causes chlorine (3) or bromine to oxidize arsenic to orthoarsenic acid.



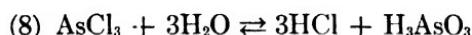
Acids do not attack arsenic readily unless the acid has oxidizing properties, *e. g.*, dilute nitric acid (4), concentrated nitric acid (5), or hot concentrated sulfuric acid (6).



Arsenic is also readily reacted upon by sodium hypochlorite solution (7).



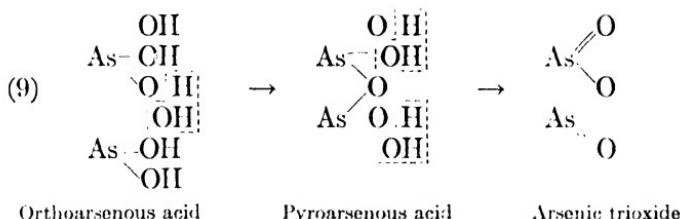
2. *Trivalent arsenic* is one of the common forms of this element. Although arsenic is classified as a non-metal, it has the ability to form a limited number of compounds in which it acts as a cation. Of these, the halides, *e. g.*, arsenic trichloride ( $\text{AsCl}_3$ ), are the outstanding examples. Even in these cases it is better regarded as an acid chloride because it is decomposed quantitatively by excess water to form orthoarsenous acid (8).



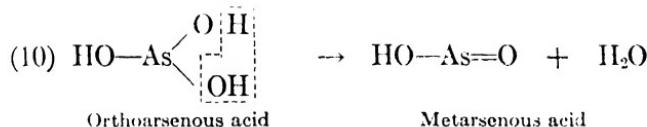
The above reaction is a reversible one in that if the concentration of HCl is increased the reaction is forced to the left and the solution will contain mostly arsenic trichloride. It is interesting to note that a hydrochloric acid solution of orthoarsenous acid, when evaporated, gives off vapors of arsenic trichloride until no arsenic remains. This is not true of a hydrochloric acid solution of orthoarsenic acid in which arsenic exists in the pentavalent form.

Graphic formulæ show the relationships of the oxides, sulfides and acids of arsenic much better than the conventional molecular

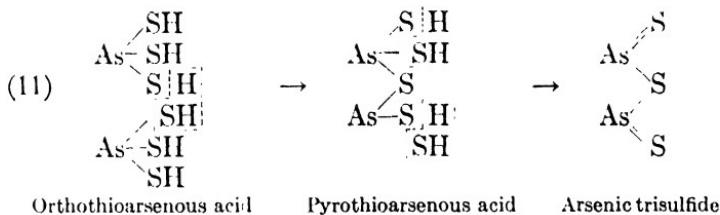
formulæ. For example, arsenic trioxide is the product of dehydration of orthoarsenous acid (9).



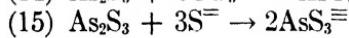
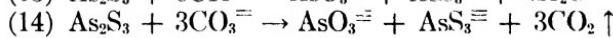
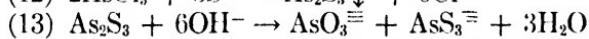
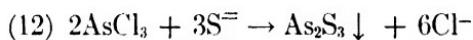
The above may be regarded as an *intermolecular* dehydration. On the other hand, one may consider *intramolecular* dehydration, wherein metarsenous acid is formed (10).



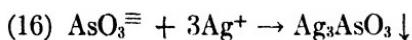
Arsenic trisulfide is exactly analogous to arsenic trioxide and is formed by the *intermolecular* dehydration of the orthothioarsenous acid (11).



1. When hydrogen sulfide is passed into an acidulated (HCl) aqueous solution of an arsenous compound, yellow arsenous sulfide is precipitated (12). The precipitate is insoluble in concentrated hydrochloric acid, but dissolves in the hydroxides (13), carbonates (14) and sulfides (15) of sodium, potassium and ammonium.



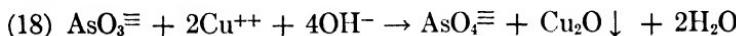
With neutral solutions of soluble arsenites, silver nitrate produces a yellow precipitate of silver orthoarsenite (16), which is soluble in an excess of ammonium hydroxide or in diluted nitric acid.



Copper sulfate precipitates from neutral solutions of arsenites green cupric hydrogen arsenite (17) (*Scheele's green*), which is soluble in ammonium hydroxide and in acids. The precipitate turns red when boiled with sodium hydroxide T.S.

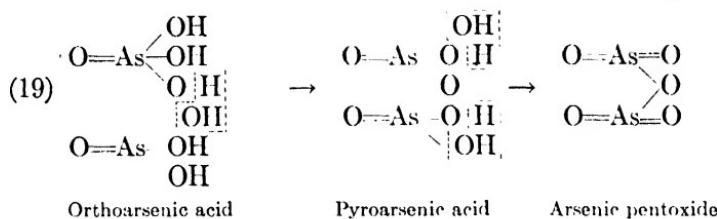


If copper sulfate and an excess of alkali hydroxide are added to a solution of an arsenite, cuprous oxide (red-brown) is precipitated and an alkali arsenate is formed (18).

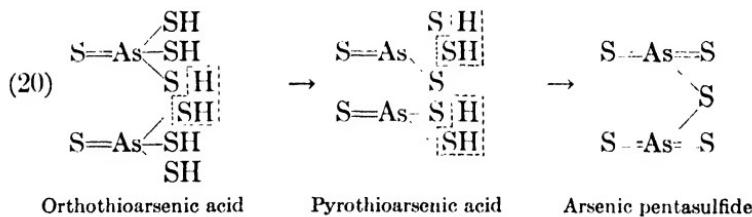


When copper acetate is added to a boiling solution of an arsenite, a green precipitate of copper aceto-arsenite is produced (See Paris Green, p. 290.)

3. *Pentavalent arsenic* is of primary interest only in that it forms certain well-defined acids, an oxide and a sulfide. Arsenic pentoxide may be considered as the anhydride of orthoarsenic acid (19) in the same way that arsenic trioxide is the anhydride of orthoarsenous acid.



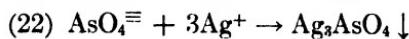
The sulfur acid, namely orthothioarsenic acid, is analogous to its trivalent counterpart (20).



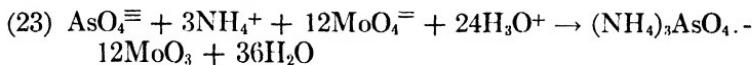
When hydrogen sulfide is passed into a hot acidulated solution of an arsenate, a yellow precipitate of arsenic pentasulfide is formed (21). The precipitate is soluble in the reagents in which arsenic trisulfide is soluble.



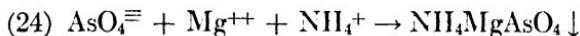
Silver nitrate, when added to a solution of an arsenate, precipitates a reddish-brown silver arsenate (22), which is soluble in ammonium hydroxide or in diluted nitric acid.



When a nitric acid solution of ammonium molybdate is warmed with a solution of an arsenate, there is produced a yellow precipitate of ammonium arsenomolybdate (23). Arsenites do not give a precipitate with this reagent.



When a small quantity of a solution of an arsenate is shaken with a clear solution of magnesium chloride, ammonium chloride, and ammonium hydroxide, a white precipitate of ammonium magnesium arsenate is formed (24). The precipitate is soluble in hydrochloric acid.



Note in the above reactions (22, 23, 24) how closely they compare with those of orthophosphoric acid (*q. v.*).

**Official Tests for Identity.**—A. *Arsenate*.—1. With silver nitrate T.S. the soluble arsenates yield a reddish-brown precipitate (22).

2. A white precipitate is obtained from arsenates with magnesia mixture T.S. (24).

This precipitate is converted to orthoarsenic acid on treatment with hydrochloric acid. This acid solution yields a precipitate of arsenic pentasulfide with hydrogen sulfide, the precipitate being soluble in ammonium sulfide T.S.

B. *Arsenite*.—1. With silver nitrate T.S. neutral solutions of arsenites yield a yellow precipitate (16).

2. Copper sulfate T.S. yields a green precipitate (17). When boiled with sodium hydroxide T.S. the precipitate becomes red in color (18).

3. Hydrogen sulfide precipitates yellow arsenic trisulfide from acidified (with HCl) solutions of arsenites (12).

**Special Reactions.**—Because arsenic at one time was used quite extensively by criminal poisoners, the detection of it in the stomach or tissues of the victim has received much attention. This accounts for the many special tests which have been proposed.

1. *Reinsch's Test*.—When a bright piece of copper is placed in an acidified (HCl) solution of arsenic and the solution heated, the copper becomes coated with a steel-gray deposit of what appears to be copper arsenide,  $\text{Cu}_5\text{As}_2$ , which can be removed by heating in a flame. Mercury and antimony interfere with this test. (See The Electromotive Series of the Metals.)

2. *Marsh's Test*.—When in solution, all soluble arsenic compounds are reduced by hydrogen (produced by the action of diluted sulfuric or hydrochloric acids on zinc) first, to arsenic and then, to arsenous hydride or arsine ( $\text{AsH}_3$ ) (25) (26) (27). Arsine burns in air with a bluish-white flame to form arsenous oxide ( $\text{As}_2\text{O}_3$ ) and water (28) or arsenic and water (29). When arsine is heated, it easily breaks down into its constituent elements. If arsine is burned from a jet, the inner or reducing flame contains free arsenic, which will deposit

as a brownish-black stain having a metallic appearance upon a cold porcelain dish held in the flame. An arsenic stain is soluble in a solution of sodium hypochlorite, whereas a similar stain produced by antimony is insoluble. Marsh's test (described below) is founded upon the chemical reaction represented by equation (30).

- $$(25) \text{AsO}_3^{\equiv} + 3\text{Zn} + 9\text{H}_3\text{O}^+ \rightarrow 3\text{Zn}^{++} + 12\text{H}_2\text{O} + \text{AsH}_3 \uparrow$$
- $$(26) \text{AsO}_4^{\equiv} + 4\text{Zn} + 11\text{H}_3\text{O}^+ \rightarrow 4\text{Zn}^{++} + 15\text{H}_2\text{O} + \text{AsH}_3 \uparrow$$
- $$(27) \text{As}^{+++} + 3\text{Zn} + 3\text{H}_3\text{O}^+ \rightarrow 3\text{Zn}^{++} + \text{AsH}_3 \uparrow + 3\text{H}_2\text{O}$$
- $$(28) 2\text{AsH}_3 + 3\text{O}_2 \rightarrow \text{As}_2\text{O}_3 + 3\text{H}_2\text{O}$$
- $$(29) 4\text{AsH}_3 + 3\text{O}_2 \rightarrow 4\text{As} + 6\text{H}_2\text{O}$$
- $$(30) \text{H}_3\text{AsO}_4 + 4\text{Zn} + 4\text{H}_2\text{SO}_4 \rightarrow \text{AsH}_3 \uparrow + 4\text{ZnSO}_4 + 4\text{H}_2\text{O}$$

The apparatus (Fig. 20) consists of a generating flask (*A*) provided with a two-hole cork (*B*). Through one of these holes is inserted a funnel-tube (*C*), extending nearly to the bottom of the flask. One end of a right-angle delivery tube (*D*) is inserted in the other hole and the opposite end connected with a drying tube (*E*) filled with calcium chloride (*F*). The drying tube, in turn, is connected to a 12-inch length of hard  $\frac{1}{4}$  inch diameter glass tubing (*G*), drawn out at 3-inch intervals to a reduced diameter of about  $\frac{1}{8}$  inch. About 3 inches from the end, the tube is drawn out to a tip.

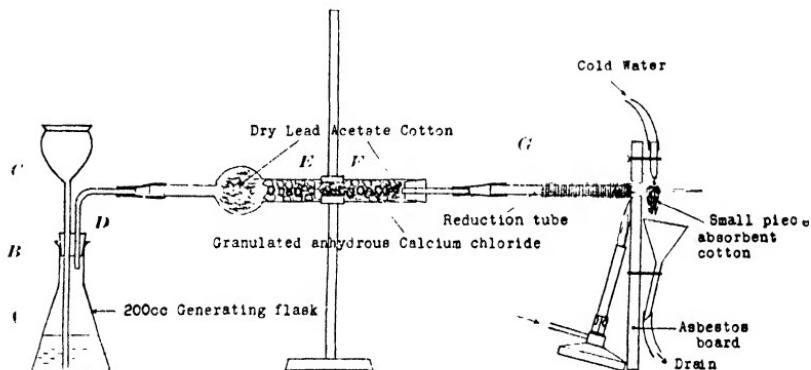


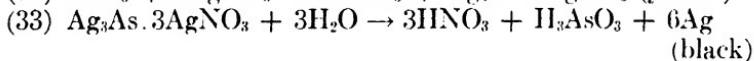
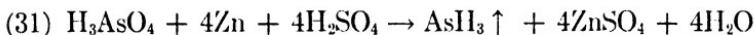
FIG. 20.—Marsh apparatus

Because sulfuric acid and zinc often contain arsenic as an impurity, the hydrogen evolved by their reaction must be tested for arsenic. A convenient quantity of zinc is placed in the flask and sulfuric acid is added. The tube (*G*) is then heated to redness at one of the wide parts for at least one-half hour. If the acid or zinc contain arsenic, a mirror will form in the constriction beyond the heated part of the tube.

When the hydrogen being generated has been proven to be arsenic-free, the solution to be tested is poured through the funnel-tube into the flask (*A*). The gas issuing from the jet is lighted, and if arsenic is present in the unknown, the flame soon becomes larger and acquires a bluish tint. A piece of cold porcelain held in

the flame is stained brownish-black. This stain may be removed with a solution of sodium hypochlorite (7). If the stain is dissolved in nitric acid, the solution evaporated to dryness, and the residue then moistened with a drop of silver nitrate solution, it becomes brick-red in color. When an antimony spot is treated in like manner, no color is produced. An arsenic mirror will be formed at a constriction in the tube if any arsine present is decomposed by heating, as directed in the test for purity of sulfuric acid and zinc.

*Gutzeit Test.*—Place about 1 Gm. of arsenic-free zinc in a test-tube, add about 5 cc. of 4 per cent arsenic-free sulfuric acid, and a small quantity (a few drops) of a neutral or acid solution of an arsenic compound (31). Cap the test-tube with several thicknesses of high grade filter paper and cover these with a third paper that has been moistened with a saturated aqueous solution of silver nitrate containing about 1 per cent of nitric acid (32). Place the tube in a dark place and, after a time, examine the paper cap. A yellow stain indicates that arsenic is present in the unknown solution. If the yellow stain is moistened with water, the color changes to a brown or black (33). Antimony compounds will cause a darkening of the silver nitrate test paper but will not give a previous yellow color.



*Modified Gutzeit Test.*—Bergeret and Merceron were the first to suggest certain changes in the so-called "Gutzeit test" for arsenic.

Certain substances interfere with the test and the chemical under examination may have to be treated specifically. The modified Gutzeit test as now used in this country is as follows:

*Preliminary Treatment.*--On account of the stain antimony hydride produces on mercuric bromide paper, and also because the salts of the heavy metals, such as bismuth, copper, iron, mercury, etc., interfere with the formation of arsine, samples containing them are best tested for arsenic by Bettendorf's method. Acid solutions of these heavy metals may be subjected also to distillation. The more volatile arsenic will be present in the distillate upon which the Gutzeit test may then be carried out.

Difficultly soluble salts, such as barium sulfate, should always be tested by Bettendorf's method. As an alternative, these salts may be suspended in water and then tested by the Marsh method.

Carbonates, on account of the carbon dioxide which would be evolved, are first treated with dilute sulfuric acid until the reaction has ceased.

The halogens also, due to their oxidizing effect, must be eliminated by heating with nitric and sulfuric acids until white fumes of sulfur dioxide are evolved. The halogens are oxidized by the nitric acid

and then expelled by the sulfuric acid. The unused nitric acid also is driven off by the heat.

Nitrogen interferes with the formation of arsine, and compounds containing it are heated with a mixture of potassium nitrate and sodium carbonate. The sodium carbonate prevents the volatilization of the arsenic. Sulfuric acid is then added, and this decomposes the carbonate and nitrates into carbon dioxide and oxides of nitrogen, respectively. These may be driven off by heat.

Organic matter prevents the evolution of arsine and is usually oxidized by incineration, using sodium carbonate to retain the arsenic. The sodium carbonate is then decomposed with dilute sulfuric acid. Oxidation by treatment with bromine solution and dilute sulfuric acid, and the subsequent treatment with potassium iodide and stannous chloride, is sometimes made use of, particularly when organic substances thus oxidized will not interfere. The stannous chloride reduces the unused halogens.

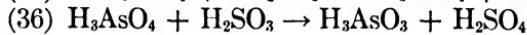
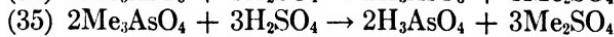
Oxidizing substances must be reduced on account of their effect upon arsine.

Phosphorus, because of the effect of phosphine, should be oxidized to the phosphate.

Sulfur compounds, owing to the darkening of the mercuric bromide paper by hydrogen sulfide, should be oxidized to the sulfate. Wherever possible, the sulfur should be driven off as hydrogen sulfide by sulfuric acid. Sometimes it is precipitated and filtered off. In general, the lead acetate paper will take care of small amounts of sulfur.

Usually, inorganic chemicals do not need any preliminary treatment.

*Preparation of Chemical.*—As certain substances interfere with this test, the chemical under examination may have to be treated specifically. The treated chemical, representing 0.2 Gm. of the original substance, is dissolved in 5 cc. of water. One cc. of a mixture of equal volumes of concentrated sulfuric acid and water is added and then 10 cc. of sulfurous acid. The mixture is evaporated on a water-bath until the volume has been reduced to 2 cc. and the liquid is free from the odor of sulfur dioxide. In the presence of sulfuric acid, arsenites are converted into arsenous acid (34) whereas arsenates are changed to arsenic acid (35), as the case may be. The sulfurous acid treatment serves to reduce any arsenic acid so formed to the trivalent arsenous state in which form it is necessary for the successful production of arsine (36).



*Apparatus.*—The generator consists of a bottle (*C*) of 50 cc. capacity, an exit tube (*B*) and a tube (*A*). (Fig. 21.) A pledget of dry glass wool is placed in the lower part of the tube (*B*), then a strip of *freshly* prepared but dry lead acetate paper and above this

is inserted a plegget of glass wool moistened with lead acetate solution. The lead acetate serves to retain any hydrogen sulfide as lead sulfide. When the test is ready to be made, a strip of mercuric bromide paper is inserted in tube (A). The mercuric bromide paper is made by dipping filter paper for five minutes in an alcoholic solution of mercuric bromide and then drying it. *It is very important that the test paper should be freshly prepared.*

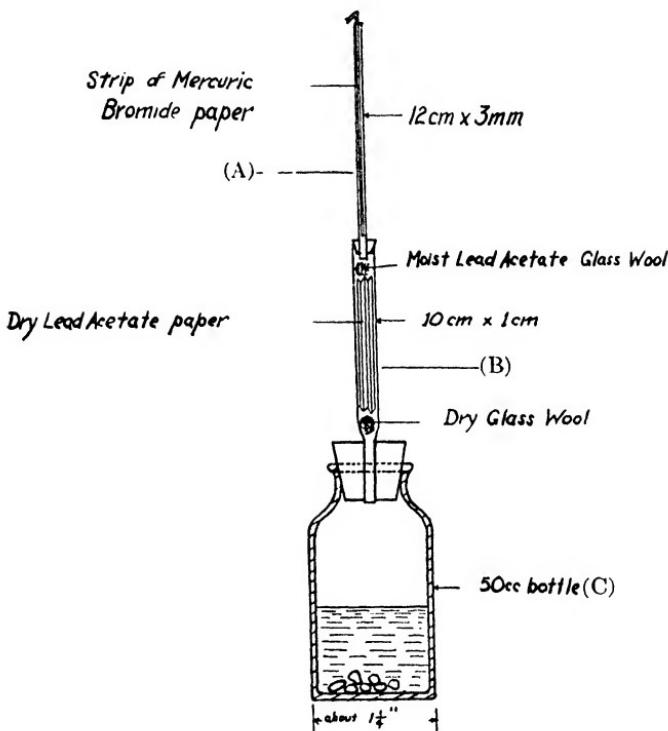
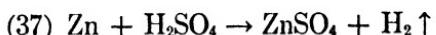


FIG. 21.—Gutzeit apparatus.

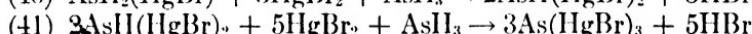
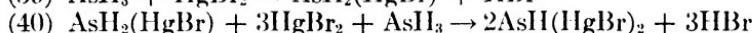
*The Test.*—About 10 Gm. of arsenic-free zinc, 25 cc. of 20 per cent sulfuric acid and 3 to 5 drops of acid stannous chloride solution are introduced into the bottle (C). The stannous chloride maintains the arsenic in a reduced state during the reaction. The solution to be tested is then added and the stopper holding the exit tubes (A) and (B) immediately inserted. The zinc and sulfuric acid react to produce hydrogen (37). The hydrogen in turn reduces the arsenous acid present to arsine (38).



When the evolution of hydrogen has proceeded actively for forty-five minutes, the mercuric bromide paper is removed. The stain produced should not exceed in length and depth of color that pro-

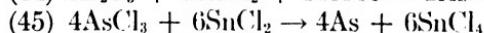
duced in like manner by 0.002 mg. (2 parts per 1,000,000) of arsenic trioxide.

As in the method described previously, a blank should be run to determine the purity of the reagents. Small quantities of stibine ( $SbH_3$ ) will not affect the mercuric bromide paper. However, larger quantities produce a brown stain very similar to that made by arsine. If the test paper is immersed in alcohol, the antimony stain disappears, whereas the yellow arsenic stain becomes distinctly brighter. The following equations have been suggested<sup>1</sup> to represent the reactions taking place between arsine and mercuric bromide. With a small amount of arsenic, the yellow stain, bromomercurarsine,  $AsH_2(HgBr)$ , will be produced (39). If more arsenic is present the orange di- and brown tri-bromomercurarsine stains (40) (41) will be formed in proportion to the arsine evolved. With an excess of arsenic, the black stain due to arsenic mercuride amalgam will be obtained (42).

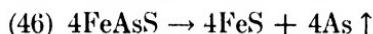


*Bettendorf's Test.*.—To a solution of an arsenic compound in concentrated hydrochloric acid, add an equal volume of a freshly prepared saturated solution of stannous chloride in concentrated hydrochloric acid and set the mixture aside for thirty minutes. A brown color or precipitate indicates the presence of arsenic (43) (44) (45). Easily reducible metals, *e. g.*, gold, mercury, selenium and tellurium, produce similar reactions to that of arsenic. Antimony and bismuth compounds do not interfere as they are not reduced to the metals. Bettendorf's test should be used to detect arsenic in the presence of antimony.

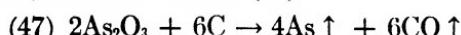
This test depends upon the reduction of arsenic ( $As^{\text{v}}$  slowly) and arsenous compounds to elemental arsenic by means of stannous chloride.



**Commercial Manufacture.**—Arsenic is prepared by roasting arsenopyrite out of contact with air (46). The vapors are condensed between rolls of sheet iron and collected in an earthenware receiver. A residue of iron sulfide is left in the retorts.



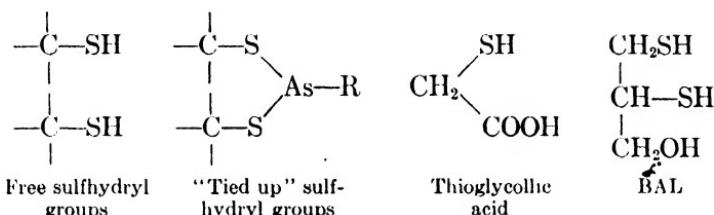
In the smelting of copper ores, arsenic trioxide collects as a dirty powder in the flues. When this is mixed with powdered coke and heated, arsenic sublimes (47).



<sup>1</sup> Partheil: Arch. d. pharm., 237, 121 (1899) (equations with mercuric chloride).

Arsenic may be purified by sublimation with powdered charcoal.

**Pharmacological Action of Arsenic Ions.**—Compounds of arsenic injure or destroy all cells and, therefore, are protoplasmic poisons. The difference in toxicity of inorganic compounds containing arsenous ions and arsenic ions is not great for mammals, but for protozoa, bacteria and yeasts the former ( $\text{As}^{\text{III}}$ ) is generally much more toxic than the latter ( $\text{As}^{\text{V}}$ ). This is also true of organic compounds containing ionizable arsenic. The toxicity<sup>1</sup> of arsenic upon cells has been shown quite conclusively to be due to a "tying up" effect that it has on —SH (sulphydryl) groups in the tissues. These sulphydryl compounds, of which *thioglycollic acid* and *glutathione* are typical examples, are essential to normal oxidation-reduction in the tissues.



This knowledge led research workers to the idea that possibly the use of simple dithiol compounds (those which contain sulphydryl groups) as competitors for the arsenic might serve to prevent a toxic reaction. This idea proved to be successful and subsequent work brought out 2,3-dimercapto-propanol (also known as BAL which is the abbreviation of British Anti-Lewisite) as an effective neutralizing agent for arsenical war gases, *e. g.*, "lewisite." Following its use for this purpose, the compound was used with marked success in the treatment of arsenic poisoning from other causes. Its use has been extended to the treatment of gold and mercury poisoning with encouraging results.

The fact, brought out above, that protozoa are much more susceptible to trivalent arsenic than are mammals, explains the widespread use of arsenic in the treatment of syphilis, a protozoan infection. It will be noted that the inorganic arsenicals are unsuited for antisyphilitic treatment because they cannot be administered in sufficient quantity to kill the protozoa without harming the host. Furthermore, it is important to note that pentavalent arsenicals must be reduced to the trivalent form in order to exert the characteristic arsenic effects.

Arsenic is eliminated from the system by the urine, feces, perspiration, milk and epithelium. Long-continued use of arsenic results in a resistance of the intestinal mucosa to the inflammatory action of arsenic. Consequently, there is much less absorption. Individuals who have developed such a tolerance for the drug can take with impunity doses which would produce very serious toxic reactions in ordinary persons.

<sup>1</sup> Am. Prof. Pharm., 13, 251 (1947).

Inorganic arsenic compounds cause dilatation and increased permeability of the capillaries, particularly in the visceral region. This action results in circulatory changes which disturb the normal functions of various organs. Small doses of arsenic compounds induce these reactions in a very mild form and, therefore, may be stimulating to the formation of new tissue. Hence, arsenic preparations are used for their supposed alterative or tonic effects and in the treatment of anemias, skin diseases, etc.

Because arsenicals are not precipitants for albumin, local applications produce only slight irritation. However, the cells are slowly killed by continuous exposure to them. These facts are responsible for the use of arsenicals to kill nerves in teeth and for the treatment of epitheliomas, rodent ulcers, warts, etc.

**Uses.**—Arsenic is used in making drugs, dyes and glass. It forms alloys with many metals. Lead containing about 0.5 per cent of arsenic has been used for making harder and more spherical shot.

#### OFFICIAL ARSENIC COMPOUNDS

##### ARSENIC TRIODIDE

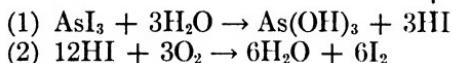
###### *Arsenic Triiodide*, N. F. VIII

Formula,  $\text{AsI}_3$ . Molecular Weight, 455.67

**Physical Properties.**—Arsenous Iodide occurs in shining orange to red crystalline scales or powder. It has a specific gravity of 4.39 at  $13^\circ \text{ C.}$ , melts at  $146^\circ \text{ C.}$ , and boils at  $400^\circ \text{ C.}$

One Gm. of arsenous iodide dissolves with almost complete hydrolysis in about 12 cc. of water at  $25^\circ \text{ C.}$  It is soluble in alcohol, in chloroform, in ether, and in carbon disulfide.

**Chemical Properties.**—Arsenous iodide is slowly hydrolyzed by water to form arsenous acid and hydriodic acid (1). Its aqueous solutions gradually turn yellow, due to the liberation of iodine (2).

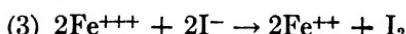


Arsenous iodide is stable at  $100^\circ \text{ C.}$ , but at higher temperatures it volatilizes.

**Official Tests for Identity.**—1. To a 1 in 50 aqueous solution of the compound add 10 cc. of hydrogen sulfide T.S. A yellow precipitate of arsenic trisulfide forms (see p. 513).

2. The addition of ferric chloride T.S. to an aqueous solution of the compound (1 in 50) causes the liberation of iodine which is detected with starch T.S.

The HI which is formed by the hydrolysis of arsenic triiodide (1) acts as an efficient reducing agent toward the ferric ion which is an oxidizing agent. This causes the formation of free iodine (3).



**Commercial Manufacture.**—1. Arsenous iodide is made by fusing together 1 part of arsenic and 5 parts of iodine and pouring the melt upon a porcelain slab to cool. The resulting product does not have a uniform chemical composition. Therefore, it is either powdered, extracted with chloroform and the resulting solution of arsenous iodide evaporated, or it is heated above 100° C. in a retort and the volatilized arsenous iodide condensed in a suitable vessel.

2. It is also made by gradually adding arsenic to a solution of iodine in carbon disulfide and digesting the mixture until the purple color of the iodine has disappeared. The carbon disulfide is distilled off and the arsenous iodide recrystallized from alcohol.

3. When a 4 per cent solution of arsenous oxide in concentrated hydrochloric acid is poured into a concentrated aqueous solution of potassium iodide (51 Gm. in 40 cc.), arsenous iodide is precipitated. The precipitate is washed with hydrochloric acid (specific gravity, 1.12) and dried.

**Pharmaceutical Preparations and Uses.**—1. *Arsenic Triiodide* (Arseni Triiodidum, Arsenous Iodide), N. F. VIII.—“Arsenic Triiodide, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of  $\text{AsI}_3$ .” The N. F. cautions: *Arsenic Triiodide is extremely poisonous.* It is used principally as an alterative tonic.

Despite numerous researches the mechanism whereby arsenic compounds act is not well understood. However, it is believed by many that compounds of inorganic arsenic, particularly when administered in small doses over a period of time, will bring about improvement in appetite and an increase in weight. This is the basis for its use in tonics and is supported more by popular opinion than by any scientific evidence. For want of a better or more specific term, this type of preparation is usually termed an “alterative.” Average dose—5 mg. (approximately  $\frac{1}{2}$  grain).

2. *Arsenic and Mercuric Iodides Solution* (Liquor Arseni et Hydrargyri Iodidorum, Donovan’s Solution), N. F. VIII.—(See p. 406.)

### ARSENIC TRIOXIDE

*Arsenic Trioxide*, U. S. P. XIII

Formula,  $\text{As}_2\text{O}_3$ . Molecular Weight, 197.82

**Physical Properties.**—Arsenic Trioxide occurs as a white powder, or in irregular masses of two varieties, *viz.*: (1) amorphous, transparent, colorless, odorless, glassy masses, sometimes called the “vitreous” or “glassy” variety; and (2) crystalline (octahedral), opaque, white, odorless masses known as the “porcelain” variety. When the “glassy” variety is exposed to moist air, it gradually becomes opaque, due to crystallization. At 800° C., the vapor density of arsenic trioxide corresponds to the formula  $\text{As}_4\text{O}_6$ , but for convenience and because this molecule dissociates into  $\text{As}_2\text{O}_3$  at 1800° C., the formula is written  $\text{As}_2\text{O}_3$ .

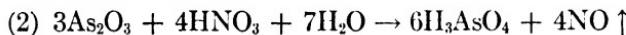
*Arsenic trioxide is very poisonous*, hence, great care should be exercised in tasting and handling it.

All forms of arsenic trioxide are slowly soluble in water. The amorphous variety is slightly more soluble than the crystalline variety, 1 part of the former dissolving in about 27 parts of water, whereas 1 part of the latter dissolves in about 59 parts of water. Because of the formation of orthoarsenous acid, both solutions give faintly acid reactions to litmus. Arsenic trioxide is slightly soluble in alcohol and in ether, and freely dissolves in glycerin. Hydrochloric acid and solutions of alkali hydroxides and carbonates dissolve arsenic trioxide.

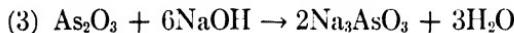
**Chemical Properties.**—When this oxide is dissolved in water it forms orthoarsenous acid as indicated above (1).



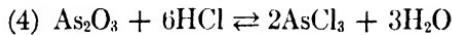
This oxide can be converted to orthoarsenic acid by heating it with dilute nitric acid (2).



As would be expected of an anhydride of an acid, it is acted upon by alkali hydroxides such as sodium hydroxide (3).



Hydrochloric acid reacts with it to form arsenic trichloride (4) (see also p. 512).



**Official Tests for Identity.**—1. Dissolve arsenic trioxide in water with the aid of heat and add hydrogen sulfide T.S. The solution becomes yellow. A few drops of hydrochloric acid added to the yellow mixture causes precipitation of arsenic trisulfide (yellow) (see also p. 513).

**Commercial Manufacture.**—Arsenic trioxide is usually obtained as a by-product in the roasting of copper, tin, cobalt and nickel ores. The fumes are passed through a series of chambers in which the arsenic trioxide collects as a dirty powder. It is purified by resublimation from iron vessels, connected by flues with condensing chambers. The arsenous oxide condenses in the first part of the apparatus as the amorphous variety and in the chamber as a crystalline powder.

**Pharmaceutical Preparations and Uses.**—1. *Arsenic Trioxide* (Arseni Trioxidum, Arsenious Acid, Arsenious Oxide), U. S. P. XIII.—Arsenic Trioxide, when dried at 100° C. for three hours, contains not less than 99.5 per cent of  $\text{As}_2\text{O}_3$ . The U. S. P. cautions: *Arsenic Trioxide is extremely poisonous*. Arsenic trioxide is employed as a tonic and alterative.

2. *Arsenic Trioxide Tablets* (Tabellæ Arseni Trioxidi, Arsenous Acid Tablets), N. F. VIII.—“Arsenic Trioxide Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of

the labeled amount of  $\text{As}_2\text{O}_3$ ." These tablets provide a convenient means of orally administering arsenic trioxide, and are usually supplied as 2-mg. tablets. Average dose—2 mg. (approximately  $\frac{1}{30}$  grain) of Arsenic Trioxide.

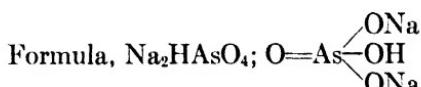
3. *Arsenious Acid Solution* (Liquor Acidi Arseniosi, Hydrochloric Solution of Arsenic, Arsenic Chloride Solution), N. F. VIII.— "Arsenious Acid Solution contains, in each 100 cc., the equivalent of not less than 0.975 Gm. and not more than 1.025 Gm. of  $\text{As}_2\text{O}_3$ ." It is made by adding diluted hydrochloric acid (50 cc.) to distilled water (250 cc.), and then adding arsenic trioxide (10 Gm.) to the acidified water. The mixture is boiled to dissolve the oxide, cooled, and made up to 1000 cc. with distilled water. As previously shown (see p. 512), arsenic trioxide dissolves in the acid to form arsenic trichloride (4), which in turn is hydrolyzed by water to form arsenous acid and hydrochloric acid. A mixture of arsenic trichloride, orthoarsenous acid, and hydrochloric acid is probably present in this solution. If it is heated to remove the water, the equilibrium is disturbed and the final product will be arsenic trioxide.

This preparation is an aqueous solution that can be used to obtain the therapeutic effect of arsenic. Pharmaceutically, it is important to note that it is acidic in nature, and for this reason lends itself to use with acidic medicaments without incompatibility. In case an incompatibility is encountered it may be advisable to use the pharmaceutical antipode of this preparation, namely *Potassium Arsenite Solution*, U. S. P. XIII. (See immediately below.) Average dose—0.2 cc. (approximately 3 minims).

4. *Potassium Arsenite Solution* (Liquor Potassii Arsenitis, Fowler's Solution, Solutio arsenicalis seu Fowleri P.I.), U. S. P. XIII.— "Potassium Arsenite Solution contains, in each 100 cc., the equivalent of not less than 0.95 Gm. and not more than 1.05 Gm. of  $\text{As}_2\text{O}_3$ ." It is made by boiling potassium bicarbonate (7.6 Gm.) and arsenic trioxide (10 Gm.) with distilled water until solution is effected. A small amount of alcohol is added (30 cc.) and the solution made up to 1000 cc. with distilled water. As noted above, this preparation may be used for the therapeutic effect of the arsenic present, and may be used, because it is alkaline, wherever incompatibility exists with an acid solution. The interchanging of the two solutions to avoid incompatibilities, of course, requires the approval of the physician. Average dose—0.2 cc. (approximately 3 minims).

## DISODIUM HYDROGEN ORTHOARSENATE

*Exsiccated Sodium Arsenate*, N. F. VIII



Molecular Weight, 185.91

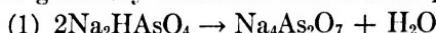
**Physical Properties.**—Exsiccated Sodium Arsenate is an odorless, amorphous, white powder. It is slightly hygroscopic.

One Gm. of Exsiccated Sodium Arsenate is soluble in about 3.5 cc. of water at 25° C. and in about 1.5 cc. of boiling water. The salt is slightly soluble in alcohol at 25° C., and is nearly insoluble in boiling alcohol.

Sodium arsenate may be crystallized in colorless, transparent, odorless, monoclinic prisms having 7 molecules of water of crystallization. In dry air the crystals effloresce, and in a moist atmosphere they deliquesce slightly.

Because of its *very poisonous character*, the salt should be tasted with caution.

**Chemical Properties.**—At high temperatures the dried salt fuses and is gradually converted into sodium pyroarsenate (1).



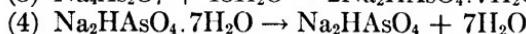
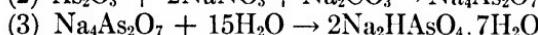
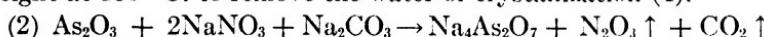
Because it is a salt of a strong base and a relatively weak acid, solutions of it have a slightly alkaline reaction due to hydrolysis.

For a more extended discussion of the reactions of the arsenate ion see p. 514.

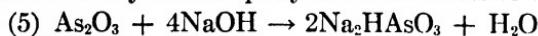
**Official Tests for Identity.**—1. It responds to all of the tests for *Sodium Ion* (*q. v.*).

2. It also responds to all of the tests for *Arsenic Ion* (*q. v.*).

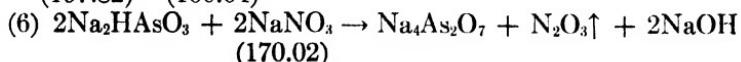
**Commercial Manufacture.**—Finely powdered arsenic trioxide, sodium nitrate, and dried sodium carbonate are thoroughly mixed and heated to dull redness in a large, clay crucible provided with a cover (2). When effervescence has ceased and complete fusion has taken place, the melt is poured on stone slabs to cool. While still warm the solidified mass is dissolved in hot water and the solution boiled with constant stirring (3). The solution is filtered and allowed to crystallize. The crystals are separated from the mother liquor and washed in a centrifuge with a fine spray of water, and rapidly dried. The crystals are heated to constant weight at 150° C. to remove the water of crystallization (4).



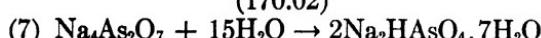
**Laboratory Preparation of Crystalline Salt.**—Dissolve 17.7 Gm. of sodium hydroxide (90 per cent) in 100 cc. of distilled water, add 20 Gm. of arsenic trioxide and boil the solution until the latter is dissolved (5). Evaporate the liquid to dryness and mix the residue thoroughly with 17 Gm. of sodium nitrate. Fuse the mixture at dull red heat (6) and pour the melt on a stone slab to cool. While still warm, dissolve it in 200 cc. of hot water and boil for one-half hour (7), replacing from time to time the water lost by evaporation. Filter the solution and evaporate to crystallization. Separate the crystals and dry them rapidly between sheets of bibulous paper.



(197.82) (160.04)



(170.02)



**Pharmaceutical Preparations and Uses.**—1. *Exsiccated Sodium Arsenate* (Sodii Arsenas Exsiccatus, Dried Sodium Arsenate), N. F. VIII.—“Exsiccated Sodium Arsenate, when dried to constant weight at 150° contains not less than 98 per cent of Na<sub>2</sub>HAsO<sub>4</sub>.<sup>1</sup>” As previously pointed out, the compound is exceedingly poisonous and, therefore, should be handled with care.

This salt represents a pentavalent inorganic arsenic compound, but in all likelihood the arsenic is reduced in the body to the trivalent form prior to exerting its action.

Because of its poisonous nature, sweetened solutions of the salt are used to kill flies and ants.

For further information on the inorganic arsenicals, see p. 521.  
Average dose—3 mg. (approximately  $\frac{1}{20}$  grain).

2. *Sodium Arsenate Solution* (Liquor Sodii Arsenatis), N. F. VIII.—“Sodium Arsenate Solution contains, in each 100 cc., not less than 0.95 Gm. and not more than 1.05 Gm. of Na<sub>2</sub>HAsO<sub>4</sub>.<sup>1</sup>” It is prepared by dissolving 10 Gm. of exsiccated sodium arsenate in enough distilled water to make 1000 cc. of finished solution. Its uses are the same as given above for Exsiccated Sodium Arsenate. Average dose—0.2 cc. (approximately 3 minims). This represents approximately 2 mg. of Exsiccated Sodium Arsenate per dose.

## SODIUM CACODYLATE

### *Sodium Cacodylate*, N. F. VIII

Formula, Na(CH<sub>3</sub>)<sub>2</sub>AsO<sub>2</sub>.3H<sub>2</sub>O. Molecular Weight, 214.02

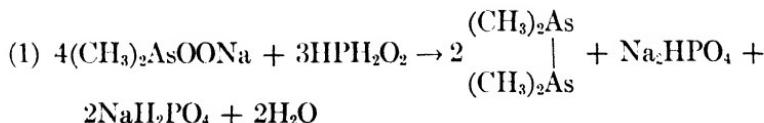
**Physical Properties.**—Sodium Cacodylate occurs in white crystals, or as a white granular powder. It is odorless and deliquescent.

One Gm. of the salt dissolves in about 0.5 cc. of water and in about 2.5 cc. of alcohol, at 25° C.

When heated to 60° C., it melts in its water of hydration and at 120° C. it becomes anhydrous. When ignited, the salt burns with a bluish flame and evolves fumes having a garlic-like odor.

**Chemical Properties.**—Sodium cacodylate, being a salt of a strong base and a weak acid, gives aqueous solutions which are alkaline to litmus paper. However, they are nearly neutral to phenolphthalein.

Sodium cacodylate in solution is readily reduced with hypophosphorous acid (1) to yield cacodyl.

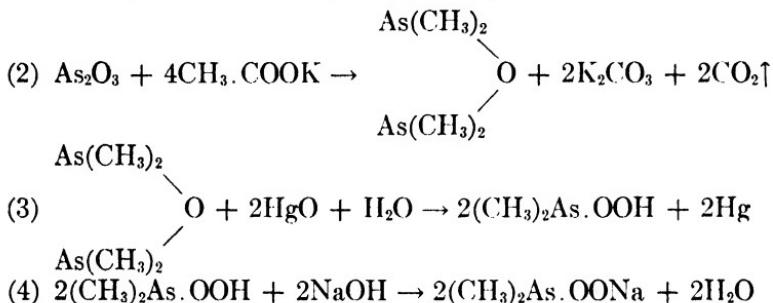


**Official Tests for Identity.**—1. Sodium Cacodylate burns with a bluish flame, emitting a garlic-like odor, and to a non-luminous flame it imparts a yellowish-orange color.

2. When a few drops of a dilute solution of the salt are added to 2 cc. of hypophosphorous acid test solution, and the mixture allowed

to stand in a stoppered flask for an hour, an odor of cacodyl will develop. This reaction involves the reduction of the sodium cacodylate by the hypophosphorous acid to cacodyl (1).

**Commercial Manufacture.**—When a mixture of arsenic trioxide and potassium acetate is distilled, a heavy, poisonous, vile-smelling, fuming oil, Cadet's liquid, is formed.<sup>1</sup> This distillate is composed chiefly of cacodyl oxide (dimethyl arsine oxide) together with some cacodyl (dimethyl arsine) (2). The oxide inflames in an atmosphere of oxygen but not in air. When cacodyl oxide is oxidized with mercuric oxide, cacodylic acid separates out in odorless prisms (3), which are freely soluble in water. The aqueous solution of the acid is neutralized with sodium carbonate or hydroxide (4), concentrated, and either crystallized or evaporated to dryness.



**Pharmaceutical Preparations and Uses.**—1. *Sodium Cacodylate* (Sodii Cacodylas), N. F. VIII.—“Sodium Cacodylate contains not less than 72 per cent and not more than 75 per cent of  $\text{Na}(\text{CH}_3)_2\text{AsO}_2$ , the remainder consisting chiefly of water.” Although sodium cacodylate is in reality an organic compound of arsenic, it is inorganic in the sense that it slowly liberates inorganic arsenic in the body. Consequently it is used in cases for which inorganic arsenic compounds are indicated (see p. 521). For a given amount of arsenic, it is comparatively much less toxic than the inorganic compounds. This drug presents an unusual feature in that its hypodermic dose (0.3 Gm.) is greater than the oral dose (0.060 Gm.). This apparent inconsistency is explained by the fact that in the acid contents of the stomach the salt reverts to the more toxic inorganic form much more readily than in the slightly alkaline blood and tissues. It has been used in the treatment of anemia, psoriasis and leukemia. Average dose—60 mg. (approximately 1 grain).

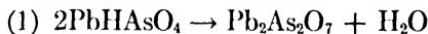
2. *Sodium Cacodylate Ampuls* (Ampullæ Sodii Cacodylatis, Sodium Cacodylate Injection), N. F. VIII.—“Sodium Cacodylate Ampuls contain a sterile solution of sodium cacodylate in water for injection, and yield  $\text{Na}(\text{CH}_3)_2\text{AsO}_2$ , equal to not less than 71 per cent and not more than 77 per cent of the labeled amount of  $\text{Na}(\text{CH}_3)_2\text{AsO}_2 \cdot 3\text{H}_2\text{O}$ .” It is interesting to note that sodium cacodylate is almost the only drug with an inorganic arsenical action that can be injected. Average dose—0.3 Gm. of Sodium Cacodylate.

<sup>1</sup> See also, J. A. C. S., 69, 559 (1947).

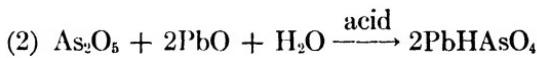
## NON-OFFICIAL COMPOUNDS OF ARSENIC

**Lead Arsenate.**—Formula  $\text{PbHAsO}_4$ , Molecular Weight, 347.13. This is a white compound which occurs as monoclinic leaflets or more commonly as an amorphous, heavy powder. It is insoluble in water, but soluble in nitric acid and in solutions of alkali hydroxides.

When heated to about  $280^{\circ}\text{C}$ . it is converted to lead pyroarsenate (1) through loss of 1 molecule of water.



It is prepared commercially by the interaction of litharge, arsenic pentoxide, and acid (2).



Whenever "lead arsenate" is mentioned without qualification, this is the salt referred to. F. C. Moulton, a chemist employed by the Gypsy Moth Commission in Massachusetts, was the first to suggest this compound as an insecticide against the gypsy moth (*Porthetria dispar*). Subsequent experience has shown it to be very effective and as a result it has come into widespread use as an insecticide.

**Hydrides.**—**Arsenic Hydride, Hydrogen Arsenide, Arsine** ( $\text{AsH}_3$ ).—Like nitrogen and phosphorus, arsenic forms a gaseous hydride, which is analogous to ammonia ( $\text{NH}_3$ ) and phosphine ( $\text{PH}_3$ ). It may be made by reducing arsenic trioxide or its compounds with nascent hydrogen (1) or by the action of dilute hydrochloric acid upon zinc or magnesium arsenide (2) (3). The gas has a garlic-like odor, is slightly soluble in water and is very poisonous when inhaled. It is decomposed into its constituent elements by passing it through a heated tube. (See Marsh's Test, p. 515.) (4.)

- (1)  $\text{As}_2\text{O}_3 + 6\text{H}_2 \rightarrow 2\text{AsH}_3\uparrow + 3\text{H}_2\text{O}$
- (2)  $\text{Zn}_3\text{As}_2 + 6\text{HCl} \rightarrow 3\text{ZnCl}_2 + 2\text{AsH}_3\uparrow$
- (3)  $\text{Mg}_3\text{As}_2 + 6\text{HCl} \rightarrow 3\text{MgCl}_2 + 2\text{AsH}_3\uparrow$
- (4)  $2\text{AsH}_3 \rightarrow 2\text{As} + 3\text{H}_2\uparrow$

**Sulfides of Arsenic.**—**Arsenic Disulfide** ( $\text{As}_2\text{S}_2$ , 213.94).—Arsenic disulfide is found in Nature in ruby-red monoclinic prisms, known as *realgar*. It is also called *red orpiment*, *ruby arsenic* and *red arsenic glass*. It is made by roasting a mixture of mispickel ( $\text{FeAsS}$ ) and iron pyrites and then subliming the product. When obtained in this manner, it is an orange-red, poisonous powder that is insoluble in water but soluble in acids and in alkalies. It is used as a depilatory in the leather industry, in pyrotechny (blue fire), in shot manufacture, in the textile industry, and as a pigment.

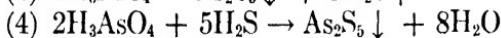
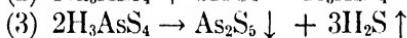
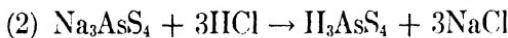
**Arsenic Trisulfide** ( $\text{As}_2\text{S}_3$ , 246.00).—Arsenic trisulfide is native in yellow rhombic prisms known as *Orpiment* or *King's Yellow* or

*King's Gold.* It may be made by passing hydrogen sulfide into a hydrochloric acid solution of arsenic trioxide (1).



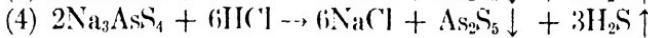
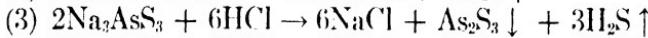
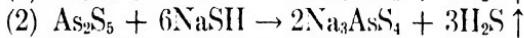
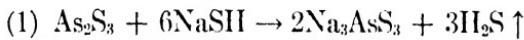
The precipitate is yellow to orange-yellow in color and is insoluble in water. It dissolves in the sulfides or carbonates of sodium, potassium, and ammonium. Arsenic trisulfide is used chiefly as a paint pigment and as a depilatory for hides.

**Arsenic Pentasulfide** ( $\text{As}_2\text{S}_5$ , 310.12).—This compound is obtained as a yellow or orange powder when thioarsenates are decomposed with an acid (2) (3), or when hydrogen sulfide is rapidly passed into an acidified (HCl) solution of arsenic acid (4).



Arsenic pentasulfide is insoluble in water, but dissolves in the reagents that dissolve the trisulfide (*q. v.*). It is used as a paint pigment.

**Thio Salts of Arsenic.**—Arsenic trisulfide ( $\text{As}_2\text{S}_3$ ) and arsenic pentasulfide ( $\text{As}_2\text{S}_5$ ) are the anhydrides of *thioarsenous acid* ( $\text{H}_3\text{AsS}_3$ ) and *thioarsenic acid* ( $\text{H}_3\text{AsS}_4$ ), respectively, and hence are analogous to arsenous oxide ( $\text{As}_2\text{O}_3$ ) and arsenic pentoxide ( $\text{As}_2\text{O}_5$ ) which are the respective anhydrides of arsenous acid ( $\text{H}_3\text{AsO}_3$ ) and arsenic acid ( $\text{H}_3\text{AsO}_4$ ). The *thio acids* of arsenic are known only in the form of their salts. Their salts may be prepared by dissolving either of the arsenic sulfides in a solution of a soluble sulfide, such as  $(\text{NH}_4)_2\text{S}$ ,  $\text{Na}_2\text{S}$  or  $\text{NaHS}$  (1) (2). When solutions of these salts are acidified, the acids immediately give off hydrogen sulfide and the sulfides are precipitated (3) (4).



## CHAPTER XXXVII

### ANTIMONY AND ANTIMONY COMPOUNDS

#### ANTIMONY (STIBIUM)

Symbol, Sb. Valence, III, V. Atomic Weight, 121.76;  
Atomic Number, 51

**History.**—This metallic chemical element, in the form of its sulfide ( $Sb_2S_3$ ), has been known from very early times. It is quite evident that, aside from using the sulfide as a cosmetic, the metal itself was obtained by the Chaldeans and used for making ornamental vessels. The Arabic and Hebrew name for native antimony sulfide was *kohl*, and Pliny mentions it as *stibium*. Geber and Basil Valentine called it *antimonium*. About the middle of the fifteenth century, Valentine not only described the metal and its method of preparation, but also discussed a number of its compounds. He also described some of the alloys of this metal and indicated the use of antimony compounds in medicine.

**Occurrence.**—Native free antimony is occasionally found in lamellar or granular masses in limestone or in mineral veins often associated with silver ores. The principal source of antimony is *antimony glance* or *stibnite* ( $Sb_2S_3$ ). Other antimony minerals are *cerantite* ( $Sb_2O_4$ ), *senarmontite* ( $Sb_2O_3$ ) and *valentinite* ( $Sb_2O_3$ ). Many of the native sulfides of copper, nickel, lead, and silver contain small amounts of antimony. Most of the world's supply of antimony comes from China. Mexico, Bolivia, Czechoslovakia and France each produce a small amount of the metal.

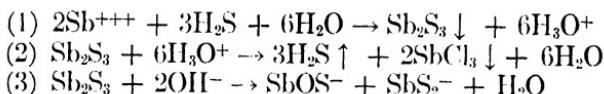
**Physical Properties.**—Antimony is a silvery-white, crystalline brittle solid, having a high metallic luster. It crystallizes in rhombohedrons and its granular or coarsely laminated crystalline structure accounts for its brittleness. When molten antimony or its alloys are allowed to cool, they crystallize and, in doing so, expand; hence, their use in making type or sharp castings. Antimony has a specific gravity of 6.68 at  $25^\circ C.$ , melts at  $630^\circ C.$  and boils at  $1440^\circ C.$  Its vapor density at  $1640^\circ C.$  corresponds to the formula  $Sb_2$ , but at lower temperatures it is apparently a mixture of  $Sb_2$  and  $Sb_4$  molecules.

Antimony exists in several allotropic forms. Besides the one just described, a modification called *explosive antimony* is known. When a solution of antimony trichloride in hydrochloric acid is electrolyzed, using an antimony anode and a copper or platinum cathode, this form is deposited on the cathode. This allotropic modification is so unstable that when it is scratched, it instantaneously and with explosive violence passes into the more stable form. This change is accompanied by the evolution of a large quantity of heat.

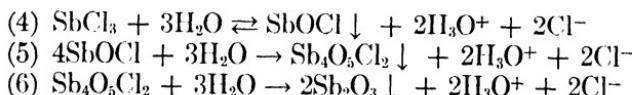
**Chemical Properties.**—At ordinary temperatures, pure antimony is quite stable in air. When heated in air or oxygen, it burns, evolving white fumes of the trioxide ( $Sb_2O_3$ ). Water does not act upon the metal, but when the latter is heated to redness it decomposes steam. Antimony combines directly with sulfur, phosphorus, and the halogens. Dilute hydrochloric acid will not dissolve antimony. When the metal is heated with concentrated hydrochloric acid, antimony trichloride is formed. Concentrated sulfuric acid slowly attacks antimony to form the sulfate  $Sb_2(SO_4)_3$  and sulfur dioxide. Concentrated nitric acid oxidizes antimony to solid antimonic acid ( $H_3SbO_4$ ).

Antimony in its trivalent state acts both as a metal and as a non-metal, whereas in the pentavalent condition, it acts only as a non-metal. The oxides and hydroxides of antimony are amphoteric, those of trivalent antimony having more pronounced basic properties than those of the pentavalent element.

Antimonous compounds in solution exhibit the following types of reactions: 1. When hydrogen sulfide is passed through a solution of an antimonous compound ( $SbCl_3$ ), an orange-red precipitate of antimony trisulfide is formed (1). The precipitate dissolves in concentrated hydrochloric acid (2), and in fixed alkali hydroxides (3).



2. When an antimonous compound is converted into the trichloride and the resulting solution concentrated and poured into water, a white, almost insoluble precipitate of antimonous oxychloride is formed (4). This is due to the hydrolysis of the trichloride. This hydrolysis is incomplete as long as any hydrochloric acid is present. The addition of more water causes further hydrolysis (5). When this latter precipitate is boiled with water, it changes to antimonous oxide (6).

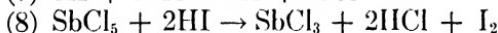
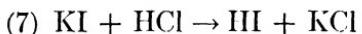


3. The addition of iron to a solution of antimony trichloride produces a brownish-black precipitate of metallic antimony. When a solution of tartaric acid and a few drops of nitric acid are added, soluble antimonyl tartrate is formed. When this solution is diluted with water to the point where the nitric acid will not oxidize hydrogen sulfide (1 to 3), and hydrogen sulfide passed into the solution, an orange-red precipitate of antimony trisulfide is produced. This test also gives a positive reaction with pentavalent antimony.

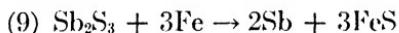
4.  $Sb^{+++}$  is reduced in acid solution by tin (or copper) and forms a coal-black metal scale which is not soluble in freshly prepared

NaBrO reagent.<sup>1</sup> For further tests, see Marsh's Test for Arsenic, p. 516.

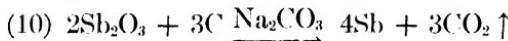
Pentavalent antimony may be identified by the use of potassium iodide. About 0.5 Gm. of the material is dissolved in 10 cc. of hydrochloric acid and the mixture warmed for several minutes at 60° to 100° C. The material is filtered and the filtrate evaporated to a volume of about 0.5 cc. The concentrated liquid is mixed thoroughly with 5 cc. of water, the precipitate allowed to settle (4), and then separated by filtration. The oxychloride is dissolved in a small amount of hydrochloric acid and a few drops of a solution of potassium iodide are added to the resulting solution (7). If pentavalent antimony is present, iodine will be set free (distinction from stannic tin) (8). Trivalent antimony will not liberate iodine in the above solution because it cannot be further reduced.



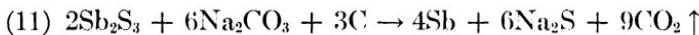
**Commercial Manufacture.**—1. Antimony is obtained by reducing finely powdered stibnite ( $\text{Sb}_2\text{S}_3$ ) with scrap iron. The molten metal is drawn off from beneath the slag of ferrous sulfide (9).



2. Large quantities of antimony are obtained by roasting the ore in air to remove sulfur and to convert the antimony into its oxides ( $\text{Sb}_2\text{O}_3$  and  $\text{Sb}_2\text{O}_4$ ). The oxides, in turn, are reduced by fusion with coal or charcoal (10).



3. Sulfide ores are often reduced by fusion with sodium carbonate and coke (11), thus:



**Pharmacological Action of Antimony Ion.**—Antimony differs in its action from arsenic by being less readily absorbed and by producing topical irritation. Otherwise, the actions of antimony very closely resemble those of arsenic. It is more caustic to the skin than arsenic, causing papular eruptions which develop into vesicular and pustular sores. The irritant action is also exerted upon the gastro-intestinal mucosa, and this results in an emetic action. When given orally in small quantities it exhibits an expectorant and a nauseant action. The salivary and bronchial glands are reflexly stimulated. Although, antimony compounds are toxic and are dangerous to use as expectorants, they are present in U. S. P. XIII and N. F. VIII preparations.

In organic combination, *e. g.*, Antimony Sodium Thioglycollate, U. S. P., and Antimony Thioglycollamide, N. N. R. 1947, antimony is used in the treatment of protozoan infections, *i. e.*, schistosomiasis,

<sup>1</sup> Noyes and Swift: Qualitative Chemical Analysis, p. 212 (1942).

leishmaniasis (kala azar), etc. These organic combinations have been found to be less toxic and less irritating than antimony potassium tartrate.

**Uses.**—Antimony is used in the preparation of its compounds, some of which (*e. g.*, tartar emetic) are used in medicine. By far the largest amount of antimony is used in the form of its alloys, of which type metal (Pb, 82 per cent; Sb, 15 per cent; Sn, 3 per cent), Babbitt metal (Sn, 80 per cent; Sb, 20 per cent), pewter (*q. v.*) and antifriction metal (Sn, 75 per cent; Sb, 12.5 per cent; Cu, 12.5 per cent) are examples. Black metallic antimony obtained by the action of zinc upon solutions of antimony trichloride is called *antimony-black* and is used to give a metallic iron or steel appearance to plaster of Paris or papier maché figures.

### OFFICIAL ANTIMONY COMPOUNDS

#### ANTIMONY POTASSIUM TARTRATE

##### *Antimony Potassium Tartrate*, U. S. P. XIII

Formula,  $K(SbO)C_4H_4O_6 \cdot \frac{1}{2}H_2O$ . Molecular Weight, 333.94

**Physical Properties.**—Antimony and Potassium Tartrate occurs as colorless, odorless, transparent crystals, or as a white powder. The crystals effloresce upon exposure to air. One Gm. of Antimony and Potassium Tartrate is soluble in 12 cc. of water and in about 15 cc. of glycerin, at 25° C. One Gm. of it is soluble in about 3 cc. of boiling water. It is insoluble in alcohol.

**Chemical Properties.**—In aqueous solution the salt turns litmus paper red (acid). This solution responds to the tests for trivalent antimony (*q. v.*) and for tartrate ion (see p. 230).

**Official Tests for Identity.**—1. Antimony potassium tartrate chars when heated, develops an odor of burning sugar, and leaves a blackened residue. This residue contains potassium carbonate and antimony trioxide which imparts an alkaline reaction to water. A piece of the residue held in a non-luminous flame produces a violet color due to the potassium.

2. A solution of the salt gives the insoluble orange-red antimony trisulfide with hydrogen sulfide (see p. 532, *e. q.*, 1, 2 and 3).

**Method of Manufacture.**—It is prepared by boiling a mixture of antimony trioxide and potassium bitartrate with water for some time. The solution is filtered, concentrated and crystallized.

**Pharmaceutical Preparations and Uses.**—1. *Antimony Potassium Tartrate* (Antimonii Potassii Tartras, Antimonyl Potassium Tartrate, Tartar Emetic), U. S. P. XIII.—Antimony Potassium Tartrate contains not less than 99 per cent of  $KOOC \cdot CHO \cdot CHOH \cdot COO(SbO) \cdot \frac{1}{2}H_2O$ . Because of its solubility and definite composition, antimony and potassium tartrate (tartar emetic) is of the greatest interest to pharmacists and physicians.

When employed as an emetic, the action (which is largely reflex)

' is slow and marked depression follows. For these reasons, its former extensive use to produce emesis has been largely discontinued. It is used largely as a depressant expectorant. The nauseant dose is about one-tenth that of the emetic dose.

Intravenous injections of antimony and potassium tartrate are of great value in the treatment of kala-azar and some other tropical diseases caused by animal parasites. Average dose—Oral, as expectorant, 3 mg. (approximately  $\frac{1}{26}$  grain); Intravenous, for tropical diseases, 30 mg., increasing to 150 mg. (approximately  $\frac{1}{2}$  to  $2\frac{1}{2}$  grains).

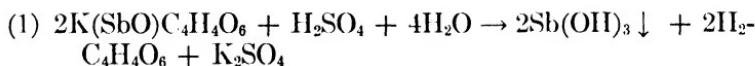
2. *Compound Opium and Glycyrrhiza Mixture* (*Mistura Opii et Glycyrrhizae Composita*, Brown Mixture), N. F. VIII.—Antimony and potassium tartrate (0.24 Gm. to 1 liter of product) is dissolved in a small quantity of hot distilled water and the solution added to glycyrrhiza fluidextract which has previously been diluted with glycerin and distilled water. Camphorated opium tincture and ethyl nitrite spirit are added, and, lastly, sufficient distilled water to make the product up to the required volume. It is extensively used alone and in combination with ammonium chloride as an expectorant cough mixture. Average dose—4 cc. (approximately 1 fluidrachm).

3. *Compound Squill Syrup* (*Syrupus Scillæ Compositus*, Hive Syrup), N. F. VIII.—Antimony and potassium tartrate (0.2 per cent) is dissolved in distilled water. The fluidextracts of squill and senega are added to the solution and the mixture allowed to stand for twelve hours with occasional shaking. The material is filtered and the sucrose dissolved by agitation in the filtrate, sufficient distilled water being added to make the required volume. The product is then mixed and strained.

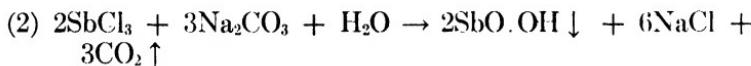
The original Cox's Hive Syrup contained honey instead of syrup. The preparation is used as an expectorant and emetic. Average dose—2 cc. (approximately 30 minims).

#### NON-OFFICIAL ANTIMONY COMPOUNDS

**Acids of Antimony.**—**Ortho-antimonous Acid** [ $H_3SbO_3$  or  $Sb(OH)_3$ ].—Ortho-antimonous acid is obtained as a white precipitate when very dilute nitric or sulfuric acid is added to a solution of antimony and potassium tartrate (1).



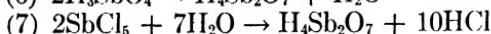
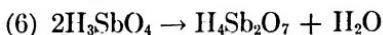
**Meta-antimonous Acid** ( $HSbO_2$  or  $SbO(OH)$ ).—Meta-antimonous acid is formed as a white precipitate when antimony trichloride is treated with a solution of an alkali carbonate or hydroxide (2). It is readily decomposed by hot water into the trioxide (3).



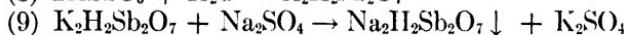
**Ortho-antimonic Acid** [ $H_3SbO_4$  or  $SbO(OH)_3$ ].—Ortho-antimonic acid is prepared by oxidizing antimony trichloride to the pentachloride with concentrated nitric acid and then diluting the solution with water (4). It is also made by the action of aqua regia upon metallic antimony (5). The gelatinous precipitate is washed and dried. It has a metallic, astringent taste and forms salts (pyro- and meta-antimonates) with fixed alkali hydroxides.



**Diantimonic or Pyroantimonic Acid** ( $H_4Sb_2O_7$ ).—This acid is obtained when ortho-antimonic acid is heated at  $100^\circ C$ . (6). It is also made by the action of hot water on antimonic chloride (7).



When antimony is fused with potassium nitrate, potassium metantimonate ( $K_2SbO_3$ ) is formed. When this is dissolved in water, it is converted into acid potassium pyroantimonate (8). When this is added to a concentrated solution of a sodium salt, acid sodium pyroantimonate is precipitated (9), which is unique by being one of the few almost insoluble salts of sodium.



**Meta-antimonic Acid** ( $H_2SbO_3$  or  $SbO_2 \cdot OH$ ).—Metantimonic acid is prepared by heating the pyroantimonic acid to  $200^\circ C$ . It is a white solid that is insoluble in water but soluble in hydrochloric acid. A basic lead metantimonate is known as *Naples yellow*. It is used as a pigment.

**Halogen Compounds.**—All of the halides of antimony, with the exception of the pentabromide, are known. They may be prepared by the direct union of the respective halogen with antimony.

**Antimony Trichloride** ( $SbCl_3$ , 228.13).—Antimony trichloride occurs as a colorless, deliquescent, crystalline solid. It is known as *butter of antimony*, *mineral butter*, etc. It has a specific gravity of 3.140 ( $\frac{25}{4}$ °), melts at  $73.4^\circ C$ . and boils at  $225^\circ C$ . It is soluble in alcohol and carbon disulfide. It may be prepared by dissolving antimony trioxide or trisulfide in concentrated hydrochloric acid and then evaporating the solution, or by distilling a mixture of powdered antimony and bichloride of mercury.

Antimony trichloride is readily hydrolyzed by water to white amorphous oxychlorides whose composition depends upon the degree of hydrolysis. When these basic or oxychlorides are dried, some  $Sb_2O_3$  is formed. This mixture is known as *Powder of Algaroth*, in allusion to its use during the sixteenth century by a famous Veronese physician, Victor Algarotus.

**Antimony Pentachloride** ( $SbCl_5$ , 299.045).—Antimony pentachloride is a colorless, hygroscopic, fuming liquid, having an unpleasant

odor. Crystals of the compound melt at 2.8° C. Its specific gravity is 2.336 at 20° C. It is made by heating the trichloride in an atmosphere of chlorine. It is hydrolyzed by an excess of water into ortho-antimonic (*q. v.*) and hydrochloric acids. When heated, it decomposes into the trichloride and free chlorine, hence its use as a chlorinating agent in organic chemistry.

**Antimony Tribromide** ( $\text{SbBr}_3$ , 361.508).—Antimony tribromide occurs in colorless, deliquescent crystals, which fuse at 96.6° C. and boil at 275° C. It is made by the action of bromine upon antimony in carbon disulfide solution. Like the trichloride, it is readily hydrolyzed by water to oxybromides. The *pentabromide of antimony* is unknown.

**Antimony Tri-iodide** ( $\text{SbI}_3$ , 502.52).—Antimony tri-iodide is formed as red-colored crystals when iodine acts upon antimony in carbon disulfide solution. It melts at about 171° C. and boils at 401° C.

**Antimony Penta-iodide** ( $\text{SbI}_5$ ).—Antimony penta-iodide is formed when antimony and an excess of iodine are heated in a sealed tube to about 100° C. It is a dark brown solid, melting at 79° C.

**Antimony Trifluoride** ( $\text{SbF}_3$ , 178.76).—Antimony trifluoride is obtained in the form of colorless or grayish-white, deliquescent prisms when antimony trioxide is dissolved in hydrofluoric acid. It melts at 292° C. The *pentafluoride* is obtained by dissolving metantomonic acid in hydrofluoric acid and evaporating the solution. It melts at 7° C.

**Hydride of Antimony.**—**Antimony Hydride**,  $\text{SbH}_3$  (Stibine).—Antimony hydride is a colorless, poisonous, unpleasant smelling gas. It is made by the reduction of antimony compounds with active hydrogen which is produced by the action of zinc and diluted sulfuric or hydrochloric acids. (See Marsh's Test, etc., p. 515.) It burns with a bluish-white flame to the trioxide. Heat decomposes stibine into its constituent elements more rapidly than it does arsine. In all other respects, however, its chemical properties closely resemble those of arsine (*q. v.*).

**Oxides of Antimony.**—There are three known oxides of antimony. The trioxide ( $\text{Sb}_2\text{O}_3$ ), which is amphoteric, *e. g.*, is capable of uniting with either acids or bases to form salts; the tetroxide ( $\text{Sb}_2\text{O}_4$ ) and the pentoxide ( $\text{Sb}_2\text{O}_5$ ) which is entirely acidic.

**Antimony Trioxide.**—Antimony trioxide occurs in Nature as the minerals *valentinitite* and *senarmontite*. Antimony trioxide is a white or slightly gray microcrystalline powder. It is odorless and tasteless, and is isomorphous with arsenic trioxide (*q. v.*). Its vapor density corresponds to the formula  $\text{Sb}_4\text{O}_6$ . When heated, it turns yellow, but on cooling, it becomes white again. At red heat (656° C.) it fuses to a yellowish liquid and volatilizes at higher temperatures. When its vapor is condensed, very small octahedral or prismatic crystals are formed.

It is very slightly soluble in water, but insoluble in alcohol, nitric acid and sulfuric acid. It dissolves in the halogen acids, in glycerin,

in warm solutions of tartaric acid, in boiling solutions of potassium bitartrate and in solutions of the caustic alkalies.

It forms two series of salts. In one of them, trivalent antimony is found as a simple cation in normal salts  $[Sb(NO_3)_3]$ , whereas in the other, the antimony occurs in the form of the *antimonyl radical*  $(SbO)^+$ ,  $[K(SbO)C_4H_4O_6]$ .

When antimony oxide is dissolved in hydrochloric acid, the solution responds to all tests for trivalent antimony (*q. v.*).

It is usually prepared by burning antimony in air or oxygen and subliming the product.

A hydrochloric acid solution of the trichloride is diluted with a large volume of water and the precipitated oxychlorides collected and digested with a 2 per cent solution of sodium carbonate until alkaline. The precipitate is then dried and ignited until free from chlorides.

The oxide can be prepared also (*a*) by heating antimony to a bright red heat in a current of steam, (*b*) by the action of nitric acid upon the metal and (*c*) by oxidizing the molten metal with litharge.

Antimony trioxide was official in N. F. V. It is infrequently used as a diaphoretic in febrile diseases and in treating trypanosomiasis. Its insolubility discourages its use. Average dose—Metric, 60 mg.; Apothecaries, 1 grain. Its chief technical use is as a powerful reducing agent.

**Antimony Tetroxide** ( $Sb_2O_4$ ).—Native as antimony ocher (*cervantite*), antimony tetroxide is a non-volatile, amorphous, white powder formed by heating the metal, the trioxide or pentoxide, the sulfide, or nitrate of antimony at about  $780^\circ$  to  $920^\circ$  C. for some time. It has a density of 6.69 and is insoluble in water and most acids. It dissolves in caustic alkalies and in hydrochloric acid. This oxide is often considered to be the antimony salt of ortho-antimonic acid ( $SbSbO_4$ ).

**Antimony Pentoxide** ( $Sb_2O_5$ ).—Antimony pentoxide is a pale yellow, insoluble powder obtained by heating antimonic acid to  $275^\circ$  C. or by treating the metal or the other oxides with concentrated nitric acid. When strongly heated (above  $450^\circ$  C.), it slowly gives up oxygen and is converted into the tetroxide. It is insoluble in water, but dissolves slowly in hydrochloric acid. Like arsenic oxide ( $As_2O_5$ ) it is acidic and upon hydrolysis forms the antimonic acids (*q. v.*).

**Antimony Sulfides.**—Three sulfides of antimony are known, *viz.*, antimony trisulfide ( $Sb_2S_3$ ), antimony tetrasulfide ( $Sb_2S_4$ ) and antimony pentasulfide ( $Sb_2S_5$ ).

**Antimony Trisulfide** ( $Sb_2S_3$ , 339.70).—Antimony trisulfide occurs in Nature as a black, lustrous, crystalline mineral known as *stibnite* or *antimonite*. Native antimony trisulfide is very soft and stains the hands like graphite. The trisulfide is formed when metallic antimony and sulfur combine and also when hydrogen sulfide is passed into an acid solution of antimony chloride or tartar emetic (1). By the latter method, an orange-red precipitate is produced which is soluble in concentrated hydrochloric acid and in alkali

sulfides. When the red sulfide is heated to above 200° C., it is changed into a gray crystalline form. An amorphous, reddish-brown variety (*kermes mineral*) may be obtained by digesting the native crystalline sulfide for several hours with a 5 per cent solution of caustic soda (2). The solution is then strained and decomposed with an excess of diluted sulfuric acid (3). The precipitate is washed thoroughly with water and dried at about 100° C.

- (1)  $2\text{SbCl}_3 + 3\text{H}_2\text{S} \rightleftharpoons \text{Sb}_2\text{S}_3 \downarrow + 6\text{HCl}$
- (2)  $\text{Sb}_2\text{S}_3 + 4\text{NaOH} \rightarrow \text{NaH}_2\text{SbO}_3 + \text{Na}_3\text{SbS}_3 + \text{H}_2\text{O}$
- (3)  $\text{NaH}_2\text{SbO}_3 + \text{Na}_3\text{SbS}_3 + 2\text{H}_2\text{SO}_4 \rightarrow \text{Sb}_2\text{S}_3 \downarrow + 2\text{Na}_2\text{SO}_4 + 3\text{H}_2\text{O}$

Antimony trisulfide is the source of a number of antimony compounds. It is used in pyrotechny and in the match industry. The orange-red variety is used in vulcanizing and coloring rubber.

**Antimony Pentasulfide** ( $\text{Sb}_2\text{S}_5$ , 403.82).—Antimony pentasulfide is sometimes called *golden antimony sulfide* or *golden sulfuret of antimony*. It is a deep orange-red powder obtained by passing hydrogen sulfide into an acidulated solution of an antimonic compound (4) or by decomposing a solution of sodium thioantimonate with hydrochloric acid (5). It is insoluble in water but dissolves in hydrochloric acid (6) and in soluble sulfides (7). When heated, it decomposes into antimony trisulfide and free sulfur.

- (4)  $2\text{SbCl}_5 + 5\text{H}_2\text{S} \rightarrow \text{Sb}_2\text{S}_5 \downarrow + 10\text{HCl}$
- (5)  $2\text{Na}_3\text{SbS}_4 + 6\text{HCl} \rightarrow \text{Sb}_2\text{S}_5 \downarrow + 6\text{NaCl} + 3\text{H}_2\text{S} \uparrow$
- (6)  $\text{Sb}_2\text{S}_5 + 6\text{HCl} \rightarrow 2\text{SbCl}_3 + 2\text{S} \downarrow + 3\text{H}_2\text{S} \uparrow$
- (7)  $\text{Sb}_2\text{S}_5 + 6\text{NaSH} \rightarrow 2\text{Na}_3\text{SbS}_4 + 3\text{H}_2\text{S} \uparrow$

Sodium thioantimonate (7) crystallizes with 9 molecules of water of hydration and in this form is known as *Schlippe's salt*. It is usually made by boiling antimony trisulfide with sulfur and sodium hydroxide.

Antimony pentasulfide is used as a pigment, in the match and fireworks industries, and for vulcanizing and coloring rubber.

## CHAPTER XXXVIII

### BISMUTH AND BISMUTH COMPOUNDS

#### BISMUTH

Symbol, Bi. Valences, III, V. Atomic Weight, 209;  
Atomic Number, 83

**History.**—In 1450, Basil Valentine described this metallic chemical element, and referred to it by the name of "wismut." Because of its brittleness, Paracelsus later designated it as a "semi-metal" and called it "wissmat." In 1546, Georgius Agricola described bismuth, suggested it as a true metal and used the names "wissmuth" and "bisemutum" and "plumbum cineareum" to designate it. Because the elementary character of bismuth was not clearly understood, it was confused with a number of other better known metals, *e. g.*, lead, zinc, tin, antimony, etc. The investigations of Johann Heinrich Pott (1739) and the accurate descriptions by Torbern Olof Bergman definitely placed the element among the metals and gave a fairly clear idea of its reactions.

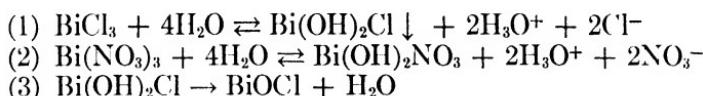
**Occurrence.**—Bismuth occurs free in Nature. The element, both free and in combination, is found disseminated in pegmatite veins and in some contact-metamorphic deposits. Most of the bismuth is obtained from the muds produced in the refining of blister copper (*q. v.*). Some of the more important bismuth minerals are *bismuth ocher* or *bismite* ( $\text{Bi}_2\text{O}_3 + (\text{H}_2\text{O})_n$ ), usually containing  $3\text{H}_2\text{O}$ , *bismutite* ( $\text{Bi}_2\text{O}_3 \cdot \text{CO}_2 \cdot \text{H}_2\text{O}$ ), *bismuthinite* or *bismuth glance* ( $\text{Bi}_2\text{S}_3$ ) and *tetradymite* ( $\text{Bi}_2\text{Te}_2\text{S}$ ). The United States produces very little bismuth. One of the world's most important deposits is located near Schneeberg, Saxony, where the bismuth is associated with cobalt minerals. Bolivia is the principal producer, although England, France, Scandinavia, Australia, United States, and Hungary also produce some of the metal.

**Physical Properties.**—Bismuth is a hard, brittle, lustrous, grayish-white metal having a reddish tint. It is usually covered with a superficial film of bismuth oxide. It has a specific gravity of 9.78 ( $20^\circ \text{ C.}$ ), melts at  $271^\circ \text{ C.}$  and boils at about  $1450^\circ \text{ C.}$  When the molten metal is cooled it crystallizes in cube-like rhombohedrons; while doing so it expands quite materially. This expansion is due to the fact that crystals of bismuth are lighter (density .9.8) than the molten metal (density, 10.055). Therefore, they must occupy a greater volume than that occupied by the same weight of the fused metal. On account of its internal crystalline structure, the metal can be powdered easily. Bismuth is a good conductor of electricity, but a poor conductor of heat.

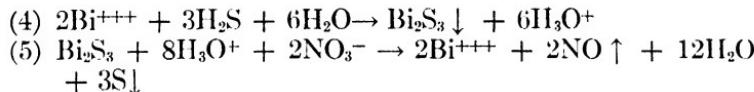
**Chemical Properties.**—Only a thin film of oxide is formed when bismuth is exposed to moist air. However, when bismuth is heated

in air, it is converted into the trioxide ( $\text{Bi}_2\text{O}_3$ ). The metal decomposes steam and combines directly with the halogens and sulfur. Only the oxyacids attack metallic bismuth to form salts. Solutions of bismuth exhibit the following types of reactions.

1. When a bismuth salt is dissolved in the least amount of diluted nitric or hydrochloric acids and water added, a white precipitate of the basic chloride or nitrate is produced (1) (2). Basic bismuth chloride loses water and is converted into the oxychloride (3). The precipitate dissolves upon the addition of acids. The presence of citric, tartaric, acetic, or other organic acids prevents the precipitation of  $\text{Bi}^{+++}$  when water is added in excess.



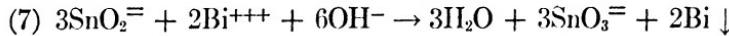
2. When hydrogen sulfide is passed into an acid solution of a bismuth salt, a brownish-black precipitate of bismuth sulfide is formed (4). This is soluble in a warm mixture of equal parts of nitric acid and water (5).



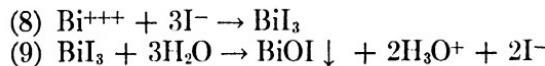
3. Alkali hydroxides precipitate white bismuth hydroxide ( $\text{Bi}[\text{OH}]_3$ ) from solutions of bismuth salts (6). The precipitate is insoluble in an excess of the precipitant.



4. When potassium or sodium hydroxide is added in excess to a solution of stannous chloride, potassium or sodium stannite is formed. When an excess of this solution is added to a solution of a bismuth salt, a black precipitate of metallic bismuth is produced (7).



5. Solutions of soluble iodides precipitate brownish-black bismuth tri-iodide from solutions of bismuth salts (8). When the precipitate is boiled with water, it is converted into the scarlet-red basic iodide (9).



**Commercial Manufacture.**—1. Native bismuth is obtained from its ore by heating the latter in inclined iron pipes. The easily fusible metal (271° C.) runs off into suitable receiving vessels.

2. Oxide and sulfide ores usually contain one or more of the following impurities: arsenic, antimony, sulfur, selenium, cobalt, nickel, iron, tin, lead, copper, etc. Such ores are first roasted to drive off sulfur and then heated in small furnaces with iron (to

combine with the remaining sulfur), charcoal (to reduce the oxides) and a flux to facilitate the operation. Metallic bismuth melts and is drawn off from underneath the lighter materials. This impure metal is usually purified by fusing it with a flux of sodium nitrate or a mixture of sodium carbonate and potassium chlorate, whereby the As, Sb, Fe, Pb, S, etc., are removed.

3. Bismuth is usually present as an impurity in lead ores, from which it is separated by an electrolytic process. All of the metallic bismuth produced in the United States is a by-product from the manufacture of electrolytic lead.

**Pharmacological Action of Bismuth Ion.**—Soluble, inorganic bismuth compounds are protoplasmic poisons and, therefore, are not used in medicine.

Because of their fineness, insolubility, and density, the insoluble bismuth compounds adhere to mucous surfaces and inflamed areas. They are employed as protectives. When taken internally, a very small amount of the bismuth goes into solution and then exerts a mild astringent and antiseptic action. The basic bismuth salts are very efficient, non-irritant intestinal antiseptics. Intestinal hydrogen sulfide acts upon basic bismuth salts to form bismuth sulfide; hence the black stools during bismuth treatment. The slight astringent and antiseptic properties, together with the protective action, make the insoluble basic carbonate and nitrate very helpful in the treatment of diarrhea, gastritis, hyperacidity, etc. There is no evidence to show that bismuth is constipating to normal individuals.

Because of their opacity, basic bismuth salts were used for Roentgen-ray diagnosis. They have been largely displaced by barium sulfate (*q. v.*).

Insoluble bismuth compounds are used as dusting powders or in the form of ointments (30 per cent) on irritated and inflamed mucous membranes or open wounds. When applied in this manner, the secretions are absorbed and the wound heals under an aseptic protective coating.

**Uses.**—Bismuth is used in the preparation of its compounds and for making alloys. Colloidal metallic bismuth in an isotonic, sterile medium is available for use as an antisyphilitic. Alloys containing bismuth are distinctive in that they are rather hard and fusible, and expand when changing from the liquid to the solid state. The latter property makes them admirably adapted for use as type metal, for taking impressions of moulds and for stereotyping. The low melting-points of bismuth alloys are easily understood when it is recalled that "solutions (alloys) freeze below the freezing-point of the pure solvent." In the case of bismuth alloys ("solid solutions"), the metallic bismuth may be considered as the "solvent," whereas the other constituents of the alloy are "solutes." Thus, *Wood's metal*, containing 50 per cent of bismuth (melting-point, 71° C.), 25 per cent of lead (melting-point, 327.5° C.), 12.5 per cent of tin (melting-point, 231.8° C.) and 12.5 per cent of cadmium

(melting-point, 320.9° C.), melts at 60.5° C., or *considerably* below the boiling-point of water. Other similar alloys are *Rose's metal* (melting-point, 93.75° C.), *Lipowitz alloy* (melting-point, 65° C.) and *Newton's alloy* (melting-point, 94.5° C.).

### OFFICIAL BISMUTH COMPOUNDS

#### BISMUTH POTASSIUM TARTRATE

*Bismuth Potassium Tartrate*, U. S. P. XIII

**Physical Properties.**— Bismuth Potassium Tartrate is a granular, white, odorless powder, having a sweetish taste. It darkens on exposure to light. One Gm. is soluble in 2 cc. of water. It is insoluble in alcohol, in ether, in chloroform and is decomposed by mineral acids.

**Chemical Properties.**— Bismuth potassium tartrate is a compound of indefinite molecular composition. Tartaric acid has two hydroxyl groups and two carboxyl groups each of which may be attacked by bismuth. When the bismuth is located at the hydroxyl group the radical, BiO, replaces the hydrogen of the hydroxyl group. BiO is known as the *bismuthyl* or *bismutho* radical. A compound thus formed may be named bismuthotartaric acid or bismuthyl tartaric acid (note synonyms). Bismuth also replaces hydrogen in the carboxyl group in the conventional manner. The type of compound formed and the amount of bismuth present in a molecule depends upon the conditions of preparation.

A solution of the salt in water will give the reactions of the potassium ion (see p. 223) and the bismuth ion (see p. 541). Silver nitrate T.S. added to a solution of the compound produced a white precipitate ( $\text{Ag}_2\text{C}_4\text{H}_4\text{O}_6$ ). When the mixture is boiled the precipitate darkens and a silver mirror is formed.

**Official Tests for Identity.**— 1. A brownish-black precipitate is produced when ammonium sulfide T.S. is added to a solution of bismuth potassium tartrate (*q. v.*).

2. An aqueous solution imparts the violet color of potassium to a non-luminous flame.

3. A silver mirror is formed when silver nitrate T.S. is added to a solution of the compound and the mixture boiled (*q. v.*).

**Commercial Manufacture.**— This compound may be prepared either by treating a mixture of bismuth nitrate and tartaric acid with sufficient potassium hydroxide solution to dissolve the precipitate that has formed, or by dissolving bismuth tartrate in the correct amount of potassium hydroxide solution. In either case, the solution is carefully evaporated to crystallization.

**Pharmaceutical Preparations and Uses.**— 1. *Bismuth Potassium Tartrate* (Bismuthi Potassii Tartras, Potassium Bismuth Tartrate, Potassium Bismuthyl Tartrate), U. S. P. XIII.— Bismuth Potassium Tartrate contains the equivalent of not less than 60 per cent and not more than 64 per cent of Bi. A solution of the compound is

used intramuscularly in the treatment of syphilis. It is thought to be effective by combining with the sulfhydryl group (SH) in the protein of the syphilis spirochete. Average dose—Intramuscular, 0.1 Gm. (approximately 1½ grains).

2. *Bismuth Potassium Tartrate Injection* (*Injectio Bismuthi Potassii Tartratis*), U. S. P. XIII.—Bismuth Potassium Tartrate Injection is a sterile solution of bismuth potassium tartrate in water for injection or a sterile suspension of bismuth potassium tartrate in oil. It contains an amount of bismuth (Bi) equivalent to not less than 57 per cent and not more than 66 per cent of the labeled amount of bismuth potassium tartrate.

Sterilize Bismuth Potassium Tartrate Injection, when an oil suspension, preferably by Process C. Sterilize Bismuth and Potassium Tartrate Injection, when a water solution, preferably by Process C, or by Process F. (See *Sterilization Processes*, U. S. P. XIII, p. 692.) Average dose—Intramuscular, 0.1 Gm. (approximately 1½ grains).

### BISMUTH SUBCARBONATE

#### *Bismuth Subcarbonate*, U. S. P. XIII

Approximate Formula,  $[(\text{BiO})_2\text{CO}_3]_2 \cdot \text{H}_2\text{O}$ . Molecular Weight, 1038.04

**Physical Properties.** Bismuth Subcarbonate is a white or pale yellowish-white, odorless and tasteless powder having a density of 6.86. It is permanent in air but is slowly affected by light.

It is insoluble in water and in alcohol, but dissolves with copious effervescence in nitric and hydrochloric acids.

When ignited, the salt decomposes into yellow bismuth trioxide, carbon dioxide and water.

**Chemical Properties.**—The salt is of indefinite chemical composition and, therefore, the purity rubric is based upon  $\text{Bi}_2\text{O}_3$ . It is very insoluble and shows only the chemical reactions of carbonates when treated with acids (see p. 167). The resulting acid solutions contain the bismuth ion and will produce reactions which are characteristic of bismuth.

**Official Tests for Identity.**—1. Bismuth subcarbonate is completely soluble in nitric or hydrochloric acid with copious effervescence.

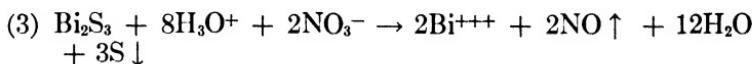
2. The solution in nitric acid or hydrochloric acid yields a white precipitate when diluted with water (1).



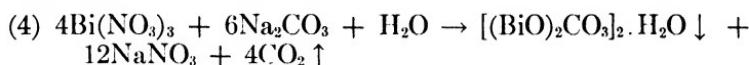
3. When hydrogen sulfide is passed into an acid solution of a bismuth salt, a brownish-black precipitate of bismuth sulfide is formed (2).



This black sulfide is soluble in a warm mixture of equal parts of nitric acid and water (3).



**Commercial Manufacture.**—Bismuth subcarbonate is made by adding an acid solution of a bismuth salt (normal bismuth nitrate) with constant stirring to a warm (not hot) solution of sodium carbonate (4). The precipitate is washed with an equal volume of cold water and dried at a temperature not above 60° C. Repeated washing of the precipitate will decompose the subcarbonate into hydroxide and therefore, should be avoided.



**Pharmaceutical Preparations and Uses.**—1. *Bismuth Subcarbonate* (Bismuthi Subcarbonas, Basic Bismuth Carbonate), U. S. P. XIII.—Bismuth Subcarbonate is a basic salt which, when dried over sulfuric acid for eighteen hours, yields on ignition not less than 90 per cent of  $\text{Bi}_2\text{O}_3$ . Bismuth subcarbonate, bismuth subnitrate and bismuth subgallate comprise the most important compounds of bismuth. Except for slight differences they all have the same therapeutic action. The compounds are used as protectives, mild astringents, dusting powders and antiseptics. Externally they are used dry or in ointment form in the treatment of ulcers and skin diseases. Internally these salts find use in gastric disorders, ulcers, diarrhea, dysentery, ulcerative colitis, etc. The subcarbonate is prescribed (either with or without supplementary antacids) when an antacid action is desired. Average dose—1 Gm. (approximately 15 grains).

2. *Bismuth Subcarbonate Tablets* (Tabellæ Bismuthi Subcarbonatis), N. F. VIII.—These tablets yield an amount of bismuth oxide,  $\text{Bi}_2\text{O}_3$ , not less than 83 per cent and not more than 97 per cent of the labeled amount of bismuth subcarbonate. Average dose—1 Gm. (approximately 15 grains).

## BISMUTH SUBGALLATE

### *Bismuth Subgallate*, N. F. VIII

Approximate Formula,  $\text{C}_6\text{H}_2(\text{OH})_3 \cdot \text{COO}(\text{BiO})$

**Physical Properties.**—It is an amorphous, bright yellow powder. It is odorless and tasteless, and is stable in the air.

Bismuth Subgallate is practically insoluble in water, in alcohol, and in ether. It is readily dissolved with decomposition by warm, moderately dilute hydrochloric, nitric, or sulfuric acid, but is insoluble in very dilute mineral acids. It is readily dissolved by solutions of alkali hydroxides, forming a clear, yellow liquid, which rapidly assumes a deep red color.

When ignited it chars leaving a yellow residue of  $\text{Bi}_2\text{O}_3$ .

**Chemical Properties.**—Bismuth subgallate is a compound of indefinite composition containing bismuth and gallic acid (3, 4, 5-tri-hydroxybenzoic acid). Here again bismuth may react with hydroxyl or carboxyl groups (see Bismuth Potassium Tartrate).

Acid solutions will respond to the reactions for bismuth ion. (See Hydrogen Sulfide Test, p. 541.) By treating the compound in water with hydrogen sulfide a small amount of bismuth sulfide is precipitated, releasing some gallic acid. The filtrate will give the characteristic purplish-blue color of the tannin test when ferric chloride T.S. is added.

**Official Tests for Identity.**—1. When heated to redness, bismuth subgallate chars, leaving yellow  $\text{Bi}_2\text{O}_3$ .

2. Bismuth subgallate responds to the test for gallic acid when treated with hydrogen sulfide T.S., filtered, and ferric chloride added to the filtrate (*q. v.*).

**Commercial Manufacture.**—It may be made by adding a warm aqueous solution of gallic acid to a solution of normal bismuth nitrate in glacial acetic acid.

**Pharmaceutical Preparations and Uses.**—1. *Bismuth Subgallate* (Bismuthi Subgallas, Basic Bismuth Gallate, Dermatol), N. F. VIII.—Bismuth Subgallate is a basic salt which, when dried at 105° for three hours, yields not less than 52 per cent and not more than 57 per cent of  $\text{Bi}_2\text{O}_3$ . It is used similarly to bismuth subcarbonate but is employed when greater astringent action is needed. Internally it finds some application in treating diarrhea. Average dose—1 Gm. (approximately 15 grains).

2. *Bismuth Subgallate Tablets* (Tabellae Bismuthi Subgallatis), N. F. VIII—These tablets yield an amount of bismuth oxide,  $\text{Bi}_2\text{O}_3$ , not less than 48 per cent and not more than 61 per cent of the labeled amount of bismuth subgallate. Average dose—1 Gm. (approximately 15 grains).

## BISMUTH SUBNITRATE

### *Bismuth Subnitrate*, N. F. VIII

Approximate Formula,  $\text{Bi}(\text{OH})_2\text{NO}_3$ . Molecular Weight, 305.02

**Physical Properties.**—Bismuth Subnitrate is a white, amorphous, slightly hygroscopic powder. It is nearly insoluble in water and insoluble in alcohol. It is dissolved by hydrochloric or nitric acids.

When bismuth subnitrate is heated to redness, it is decomposed into yellow bismuth trioxide and oxides of nitrogen (1).



**Chemical Properties.**—Bismuth subnitrate is a basic bismuth nitrate of unknown composition. The structure must be fairly constant since ignition of various batches of the salt yield between 79 and 82 per cent of  $\text{Bi}_2\text{O}_3$ .

When moistened blue litmus paper is brought in contact with basic bismuth nitrate, it turns a faint pink. This is caused by the further hydrolysis of the salt to the hydroxide and free nitric acid (2).

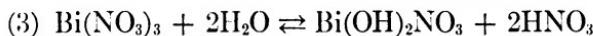


A hydrochloric or nitric acid solution exhibits the reactions of the bismuth ion (*q. v.*).

When the compound is heated with sulfuric acid and metallic copper, brownish-red fumes ( $\text{NO}_2$ ) are evolved. A hydrochloric acid solution of the salt gives the tests for the nitrate ion (see Nitric Acid, p. 120).

**Official Tests for Identity.**—Bismuth subnitrate responds to all tests for *Bismuth* ion (p. 540) and for *Nitrate* ion (p. 120).

**Commercial Manufacture.**—One part of bismuth trinitrate is rubbed to a smooth paste with 4 parts of water, and then added with constant stirring to 20 parts of boiling water. The white precipitate is allowed to subside and the supernatant liquid decanted. The precipitate is washed with an equal volume of cold water. The mixture is filtered and the basic bismuth nitrate dried at a temperature of  $30^\circ \text{ C}$ . If repeatedly washed with water, bismuth subnitrate will be converted into bismuth hydroxide (3) (4).



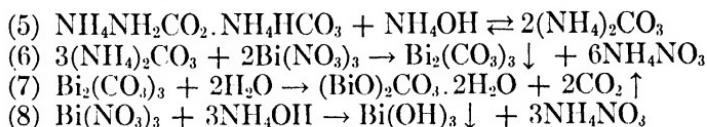
**Laboratory Preparation.**—Add a mixture of 4 cc. of nitric acid and 1 cc. of water to about 2 Gm. of metallic bismuth contained in a beaker. Heat gently until solution is effected. Evaporate the solution to about one-half its volume and add it with constant stirring to about 200 cc. of hot water. Allow the precipitate to settle, decant the supernatant liquid, and wash the salt with about its volume of cold water. Collect the precipitate and dry it at  $30^\circ \text{ C}$ .

**Pharmaceutical Preparations and Uses.**—1. *Bismuth Subnitrate* (Bismuthi Subnitrás, Basic Bismuth Nitrate), N. F. VIII.—Bismuth Subnitrate is a basic salt which, when dried over sulfuric acid for eighteen hours, yields upon ignition not less than 79 per cent of bismuth oxide ( $\text{Bi}_2\text{O}_3$ ). Like all of the basic bismuth salts, the subnitrate is a most effective non-irritant intestinal antiseptic. No doubt, its antiseptic action is due to a small amount of ionized bismuth. By virtue of a purely mechanical action, it has a marked healing effect on inflamed mucous surfaces and hence, it is used as a dusting powder for wounds. Bismuth subnitrate not only exerts this influence in the intestines, but also combines with hydrogen sulfide to form bismuth trisulfide, therefore the brownish-black color of bismuth stools. It is employed in treating gastric ulcers, etc. (See Bismuth Subcarbonate.) Average dose—1 Gm. (approximately 15 grains).

2. *Bismuth Subnitrate Tablets* (Tabellæ Bismuthi Subnitratis), N. F. VIII.—These tablets yield an amount of  $\text{Bi}_2\text{O}_3$ , not less than 73 per cent and not more than 85 per cent of the labeled amount

of bismuth subnitrate. Average dose—1 Gm. (approximately 15 grains).

3. *Bismuth Magma* (Magma Bismuthi, Milk of Bismuth, Bismuth Cream), N. F. VIII.—Each 100 cc. of this preparation contains bismuth hydroxide and bismuth subcarbonate in suspension in water, and yields not less than 5.2 per cent and not more than 5.8 per cent of  $\text{Bi}_2\text{O}_3$ . It is made by quickly adding an acidulated solution of normal bismuth nitrate to a solution of ammonium carbonate in diluted ammonia solution (5) (6) (7) (8). The magma is then washed with distilled water until free of ammonium nitrate and ammonium hydroxide.



The N. F. VIII permits of varying the method of preparation, provided the product meets the standards and tests for identity, purity and quality specified in the N. F.

It is used internally like the subcarbonate but, as a rule, is less effective. Average dose—4 cc. (approximately 1 fluidrachm).

4. *Bismuth Paste* (Pasta Bismuthi, Beck's Bismuth Paste), N. F. VIII.—This is a mixture of white wax, paraffin, and white petrolatum with 30 per cent bismuth subnitrate. This preparation is used but little, although it has been employed in tuberculous fistulas by surgical injection.

5. *Compound Resorcinol Ointment* (Unguentum Resorcinolis Compositum), N. F. VIII.—This ointment contains 6 per cent each of bismuth subnitrate, resorcinol, zinc oxide, and rectified birch tar oil, incorporated in an ointment base composed of petrolatum, yellow wax, wool fat, and glycerin. It is used to allay irritation.

6. *Bismuth Paste Surgical*, N. N. R.—This preparation contains bismuth subnitrate, 1 part, in yellow petrolatum, 2 parts.

### BISMUTH SUBSALICYLATE

*Bismuth Subsalicylate*, U. S. P. XIII

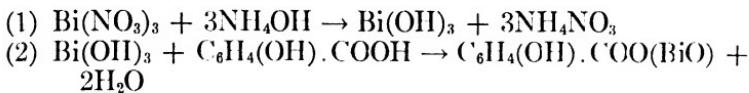
Approximate Formula,  $\text{C}_6\text{H}_4(\text{OH}) \cdot \text{COO}(\text{BiO})$

**Physical Properties.**—Bismuth Subsalicylate is a white or nearly white, amorphous, or microcrystalline, odorless powder. It is stable in air, but is affected by light. It is practically insoluble in cold water. When heated it becomes soft and chars, leaving a residue of yellow  $\text{Bi}_2\text{O}_3$ .

**Chemical Properties.**—Bismuth subsalicylate is a basic salt having an indefinite structure of bismuth and salicylic acid. When mixed with water and particularly hot water, a slow hydrolysis takes place that liberates salicylic acid and forms a more basic salt. The salicylic acid thus formed will give a deep violet-blue color

upon the addition of a few drops of ferric chloride T.S. Alcohol and glycerin cause a similar reaction. If the bismuth oxide,  $\text{Bi}_2\text{O}_3$ , that results after ignition is dissolved in nitric acid, the solution exhibits all of the reactions of the bismuth ion (*q. v.*).

**Commercial Manufacture.**—It is made by precipitating bismuth hydroxide from a solution of the trinitrate with ammonium hydroxide and then digesting the precipitate with salicylic acid on a water-bath (1, 2).



**Pharmaceutical Preparations and Uses.**—1. *Bismuth Subsalicylate* (Bismuthi Subsalicylas, Basic Bismuth Salicylate), U. S. P. XIII.—Bismuth Subsalicylate is a basic salt which, when dried over sulfuric acid for eighteen hours, yields upon ignition not less than 62 per cent and not more than 66 per cent of  $\text{Bi}_2\text{O}_3$ . It is used to allay intestinal irritation and to check diarrhea, particularly in cases of hypergastro-intestinal fermentation. A sterile suspension in a suitable fixed oil is used intramuscularly for the systemic effect of the bismuth against syphilis. Average dose—Oral, gastro-intestinal, 1 Gm. (approximately 15 grains); Intramuscular, in oil, anti-syphilitic, 0.1 Gm. (approximately  $1\frac{1}{2}$  grains).

2. *Bismuth Subsalicylate Injection* (Injectio Bismuthi Subsalicylatis), U. S. P. XIII.—Bismuth Subsalicylate Injection is a sterile suspension of bismuth subsalicylate in a suitable fixed oil. It contains an amount of bismuth (Bi) equivalent to not less than 53 percent and not more than 62 per cent of the labeled amount of bismuth subsalicylate. It meets the requirements of the Sterility Test for Liquids. Average dose—Intramuscular, 0.1 Gm. (approximately  $1\frac{1}{2}$  grains).

#### NON-OFFICIAL BISMUTH COMPOUNDS

**Bismuth Nitrate** [ $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ ].—Bismuth nitrate crystallizes in large, transparent, asymmetric prisms, having a specific gravity of 2.83 at 20° C. At 73° C., the crystals melt in their water of crystallization and upon continued heating at 80° C. the anhydrous salt decomposes into a basic nitrate, water, and oxides of nitrogen. When strongly heated, the nitrate is converted into the trioxide (*q. v.*). The normal nitrate is soluble in alcohol and in acetone. It is readily hydrolyzed by water to basic bismuth nitrate, whose composition depends upon the degree of hydrolysis. (See p. 541.)

Normal bismuth nitrate is made by dissolving 1 part of coarsely powdered metallic bismuth in 4 parts of 33 per cent nitric acid, which has been warmed previously to about 30° C. The solution is filtered through an asbestos filter (Gooch crucible) and then allowed to crystallize (1).



**Uses.**—Normal bismuth nitrate is used chiefly in the manufacture of bismuth salts, *e. g.*, the subnitrate, subcarbonate, subgallate and subsalicylate (*q. v.*).

**Sodium Iodobismuthite.**—This is sodium bismuth iodide formed by the interaction of bismuth chloride and sodium iodide in ethyl acetate solution. It is mainly  $\text{Na}_2\text{BiI}_5$ , having some inorganic salts mixed in the preparation. It contains approximately 21 per cent bismuth (Bi), 62 per cent iodide ( $\text{I}^-$ ) and 11 per cent water of hydration. Sodium iodobismuthite occurs as a red crystalline compound. It is odorless or has only a faint acetic or ethyl acetate odor. It is permanent in dry air and possesses an astringent taste. It is used intramuscularly for spirochete infections.

**Sodium Bismuthyl Citrate.**—This preparation is similar to potassium bismuth tartrate both in chemical formation and structure and is used similarly in therapeutics.

**Bismuth Sodium Tartrate, N. N. R.**—This is basic bismuth tartrate containing 72.7 to 73.9 per cent of bismuth. It is used for the systemic effect of bismuth and has been reported to be a specific for tularemia.

**Sodium Potassium Bismuthyl Tartrate, N. N. R.**—This is a basic water-soluble sodium potassium bismuth tartrate containing from 40.75 to 41.25 per cent of bismuth. It is a white, heavy powder, soluble in water and insoluble in organic solvents. Chemically, it is similar to potassium bismuth tartrate and has the same use.

**Halogen Compounds.—Bismuth Tribromide** ( $\text{BiBr}_3$ , 448.75).—Bismuth tribromide is a yellow crystalline powder which is readily soluble in diluted HCl and in 10 per cent solutions of potassium chloride, bromide, or iodide. It is decomposed by water to form basic bromides.

**Bismuth Dichloride** ( $\text{BiCl}_2$  or  $\text{Bi}_2\text{Cl}_4$ ).—Bismuth dichloride may be made by fusing the trichloride with the metal, by slowly passing a current of chlorine over the fused metal, or by heating a mixture of powdered bismuth and calomel to  $250^\circ \text{C}$ . It is a brownish-black crystalline solid. Water decomposes it into the oxychloride and metallic bismuth.

**Bismuth Trichloride** ( $\text{BiCl}_3$ , 315.37).—Bismuth trichloride was obtained by Robert Boyle by heating metallic bismuth with mercuric chloride. It may be prepared by allowing dry chlorine to act upon heated bismuth, by the action of concentrated hydrochloric acid upon bismuth trioxide, or by dissolving the metal in nitrohydrochloric acid, evaporating the solution and subliming the residue. The salt is a deliquescent, white or yellowish-white solid and is often called *butter of bismuth*. It has a specific gravity of 4.7 at  $2^\circ \text{C}$ . and melts at  $230^\circ \text{C}$ . It is decomposed at  $300^\circ \text{C}$ .

It is soluble in alcohol and in acetone. The parent compound of all bismuth salts is the trioxide. This oxide is very feebly basic, a fact that indicates that its salts would be readily hydrolyzed by water. This is the case and the hydrolysis is further stimulated

by the formation of difficultly soluble basic compounds. (See Tests for Identity, p. 544.) Therefore, when a large quantity of water is added to bismuth trichloride, a white, crystalline oxychloride ( $\text{BiOCl}$ ), known as *pearl white*, is formed. It is used as a pigment and in the manufacture of artificial pearls, etc.

**Bismuth Tri-iodide** ( $\text{BiI}_3$ , 589.76).—Bismuth tri-iodide occurs in the form of grayish-black, glistening, hexagonal crystals, having a density of 5.70 and melting at  $439^\circ\text{ C}$ . It may be obtained by fusing together the metal and iodine, or by adding a solution of a soluble iodide to an acid solution of bismuth nitrate. Bismuth tri-iodide is not affected by cold water. Boiling water changes it to the scarlet-red bismuth *oxyiodide* ( $\text{BiOI}$ ). It is completely soluble in HCl and in a 10 per cent solution of KI.

**Oxides and Hydroxides.**—Bismuth forms four oxides, *viz.*,  $\text{BiO}$ ,  $\text{Bi}_2\text{O}_3$ ,  $\text{Bi}_2\text{O}_4$ ,  $\text{Bi}_2\text{O}_5$ . Its principal hydroxide is  $\text{Bi}(\text{OH})_3$ .

**Bismuthyl** ( $\text{BiO}$ ).—Bismuthyl is a slightly basic oxide said to be formed upon the limited oxidation of the metal. This oxide enters into compounds as a univalent radical ( $\text{BiO}^+$ ), and hence is designated as *bismuthyl*.

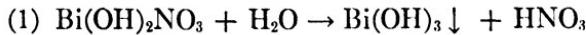
**Bismuth Trioxide** ( $\text{Bi}_2\text{O}_3$ ).—Bismuth trioxide is by far the most important oxide of bismuth. It is native as the mineral *bismuth ocher* or *bismite* ( $\text{Bi}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ ). It may be prepared by the oxidation of the metal at red heat, or by the ignition of the nitrate, carbonate, or hydroxide. When so made, it is a heavy, yellowish to brownish basic powder (specific gravity, 8.9 at  $29^\circ\text{ C}$ .). At about  $820^\circ\text{ C}$ ., it fuses to a reddish-brown liquid, which cools to a yellow crystalline mass. It is insoluble in water, but dissolves in mineral acids to form soluble normal salts which are readily hydrolyzed by water.

Bismuth trioxide is used in the preparation of bismuth salts. It is employed also in making optical glass, to which it gives even greater hardness and refractive power than is obtained by using lead.

**Bismuth Tetroxide** ( $\text{Bi}_2\text{O}_4$ ).—Bismuth tetroxide is a slightly acidic oxide formed when bismuth trioxide and potash are fused together or when bismuth trioxide, potash and potassium chlorate are ignited. It is a heavy, yellowish-brown powder (density, 5.6). The hydrate ( $\text{Bi}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ ) is known.

**Bismuth Pentoxide** ( $\text{Bi}_2\text{O}_5$ ).—Bismuth pentoxide is a brownish powder (density, 5.1) obtained by heating metabismuthic acid ( $\text{HBiO}_3$ ) (of which it is the anhydride) to  $130^\circ\text{ C}$ . The potassium salt of metabismuthic acid ( $\text{KBiO}_3$ ) is formed as a scarlet-red precipitate when bismuth trioxide is suspended in a concentrated solution of potassium hydroxide and then oxidized electrolytically or by passing chlorine through the mixture.

**Bismuth Hydroxide** [ $\text{Bi}(\text{OH})_3$ ].—Bismuth hydroxide is formed as a white amorphous precipitate when an acid solution of a bismuth salt is treated with an alkali hydroxide. Also, when basic bismuth nitrate is repeatedly washed with water, the hydroxide is formed (1).



When the trihydroxide is heated at 100° C., it loses water and is converted into  $\text{BiO(OH)}$ , a white, amorphous powder having weak basic properties. When ignited, bismuth trihydroxide is converted into the trioxide.

**Sulfides.**—Two sulfides of bismuth are known, *viz.*,  $\text{Bi}_2\text{S}_2$  and  $\text{Bi}_2\text{S}_3$ .

**Bismuth Disulfide** ( $\text{Bi}_2\text{S}_2$ ).—Bismuth disulfide is formed when an excess of metallic bismuth and sulfur are fused together.

**Bismuth Trisulfide** ( $\text{Bi}_2\text{S}_3$ ).—This sulfide occurs native as *bismuth glance* or *bismuthinite*. It may be prepared by the direct combination of the elements (sulfur in excess) or by passing hydrogen sulfide into a solution of a bismuth salt (see p. 541). It is insoluble in water and nearly so in sodium or ammonium sulfides. (See Arsenic Sulfide and Antimony Sulfide, pp. 530 and 539.) It dissolves in nitric acid. When heated to 200° C., it assumes the crystalline form of native sulfide.

## CHAPTER XXXIX

### VANADIUM, COLUMBIUM AND TANTALUM AND THEIR COMPOUNDS

#### VANADIUM

Symbol, V. Valence, II to V. Atomic Weight, 50.95;  
Atomic Number, 23

**History.**—A. M. del Rio (1801) showed the existence of a new metal in a lead ore found at Zimapán, Mexico. He called it *erythronium*, because its salts became red when heated with acids. Four years later, Collet-Descotils suggested that Rio had obtained an impure oxide of chromium. The element was rediscovered and first described by Sefström in 1830. He found it in an iron ore occurring in Sweden and named it *vanadium* from Vanadis, a cognomen of the goddess Freia. A year afterward he published the results of his investigation, described a large number of compounds of vanadium and called attention to the similarity in chemical behavior of this element to that of chromium and molybdenum.

**Occurrence.**—Vanadium is somewhat rare and forms the main part of but few minerals. It, however, is fairly widely distributed in the earth's crust and its presence has been shown in some meteorites and in the sun. The chief vanadium minerals are *patronite*, a complex vanadium sulfide, *vanadinite* ( $3\text{Pb}_3(\text{VO}_4)_2 \cdot \text{PbCl}_2$ ), *dechenite* ( $\text{Pb}, \text{Zn} (\text{VO}_3)_2$ ), *descloizite* ( $\text{Pb}_2\text{V}_2\text{O}_7$ ) and several others. The principal commercial source is Minas Ragra in the Peruvian Andes.

**Physical Properties.**—Pure vanadium is a grayish powder or crystalline mass having a silver-white luster. The metal takes an excellent polish and is permanent in air. It does not decompose water at ordinary temperatures, but the powdered metal burns like iron when heated in oxygen. Vanadium has a density of 5.87, melts at  $1715^\circ \text{C}$ . and boils at  $3000^\circ \text{C}$ . It is the hardest of all metals (about 7 on Moh's Scale).

**Chemical Properties.**—Solutions of vanadates yield with ammonium sulfide T.S. a brown precipitate which is moderately soluble in an excess of the reagent to produce a reddish-brown solution ( $\text{NH}_4\text{VS}_3$ ).

Vanadium forms five compounds with oxygen. These are  $\text{V}_2\text{O}$ ,  $\text{VO}$  (gray),  $\text{V}_2\text{O}_3$  (black),  $\text{VO}_2$  (dark blue), and  $\text{V}_2\text{O}_5$  (dark red to orange-red). Each of these oxides forms salts. The first three are entirely basic, the last two are acidic, but also possess weak basic qualities. Metavanadic acid ( $\text{HVO}_3$ ) was first obtained by Gerland. It is a yellow pigment, sometimes called *vanadium bronze*, and is used instead of gold bronze. It results as fine golden or orange scales when copper vanadate is treated with sulfurous acid. Vana-

dium bronze is obtained also by the action of copper sulfate, containing an excess of ammonium chloride, on ammonium vanadate. Vanadium also forms *pyrovanadic acid* ( $H_2V_2O_7$ ) and *hexavanadic acid* ( $H_4V_6O_7$ ). Salts of all these acids are known, as are also the salts of *orthovanadic acid*, such as  $Na_3VO_4$ .

Vanadium forms three chlorides,  $VCl_2$ ,  $VCl_3$  and  $VCl_4$ , and also the oxychlorides  $VOCl$ ,  $VOCl_2$  and  $VOCl_3$ . Some of the corresponding compounds of the other halogens are known. The vanadyl compounds, such as  $(VO)_2(SO_4)_3$ , have been prepared. Vanadium forms the nitrides  $VN$  and  $VN_2$  and the carbide  $VC$ .

**Commercial Manufacture.**—Vanadium in the pure state was first obtained by reducing its dichloride with pure hydrogen, but it is very difficult to prepare it by this method. The metal, usually in the form of an alloy, *ferrovanadium* (from 30 to 40 per cent V), is obtained by introducing the sulfide ore mixed with iron into an electric furnace, where carbon reduces the  $V_2S_5$  to V, which combines with the molten iron to form the alloy. It is also obtained by roasting the sulfide ore to drive off sulfur, fusing with sodium carbonate and leaching out the sodium vanadate so formed. By the addition of concentrated sulfuric acid, the pentoxide is precipitated, mixed with iron and, at a very high temperature, reduced to ferrovanadium.

**Uses.**—Vanadium salts have been recommended for the treatment of anemia, chlorosis, etc. However, it is very rarely, if ever, used medicinally.

It belongs to the group of metals known as the *steel elements*. It is used in making vanadium steel, which has a high tensile strength. It is employed also in the form of its compounds ( $V_2O_5Cl_4 \cdot 5H_2O$ ;  $VOSO_4 \cdot 2H_2O$ ) in the dyeing industry.

## COLUMBIUM AND TANTALUM

### Symbols, Cb and Ta

Cb: Valence III and V. Atomic Weight, 92.91; Atomic Number, 41

Ta: Valance (III), V. Atomic Weight, 180.88; Atomic Number, 73

**History.**—In the year 1801 Hatchett, an English chemist, reported to the Royal Society the results of his studies of a black mineral from Connecticut. He believed it contained a new metal which he named *columbium*. A year later Ekeberg, in Sweden, investigated a mineral from Finland, and found an element which resembled titanium, tin, and tungsten, but still was somewhat unlike any one of them. He suggested the name *tantalum* for the metal. Wollaston showed that the same element was found by both Hatchett and Ekeberg. The distinction between the two elements, columbium and tantalum, came in 1865 as a result of the work of Hermann, Blomstrand, and Marignac.

**Occurrence.**—Both columbium and tantalum are widely distributed in Nature. A few deposits are of commercial importance, such as the *samariskite* mineral in North Carolina. The metals occur

chiefly as intimate mixtures of columbates and tantalites,  $\text{Fe}(\text{CbO}_3)_2$  and  $\text{Fe}(\text{TaO}_3)_2$ . The ores are mined mainly for tantalum, since there is but little use for columbium.

**Physical Properties.**—Metallic columbium is about as hard as wrought iron, has a steel-gray color and when polished, possesses a brilliant metallic luster. It melts at  $1950^\circ \text{ C}$ . and has a density of 8.4.

Metallic tantalum is somewhat like platinum in appearance but not so bright. It is ductile, very tough, and has a tensile strength about two and one-half times that of platinum. It melts at  $2850^\circ \text{ C}$ . and has a density of 16.6. The pure metal is almost as soft as copper, but may be hardened by heat treatment, so that it will hold a cutting edge.

**Chemical Properties.**—The elements are so much alike in their chemical properties that they have been considered together. Columbium is pentavalent in most of its compounds and is sometimes trivalent. It has a strong tendency to form oxysalts. Tantalum acts almost entirely as a pentavalent element and is more basic than columbium.

Columbium forms three oxides. They are the monoxide ( $\text{CbO}$  or  $\text{Cb}_2\text{O}_2$ ), the dioxide ( $\text{CbO}_2$  or  $\text{Cb}_2\text{O}_4$ ) and the pentoxide ( $\text{Cb}_2\text{O}_5$ ). The first two are prepared from the last by reducing it with sodium and hydrogen, respectively. The pentoxide is a white, infusible powder, formed by heating columbic acid.

Columbic acid ( $\text{HCbO}_3$ ) results as a white precipitate when potassium hexacolumbate is treated with sulfuric acid. Columbates of the formulas  $\text{K}_3\text{CbO}_4$ ,  $\text{KCbO}_3$ ,  $\text{K}_4\text{Cb}_2\text{O}_7$  and  $\text{K}_8\text{Cb}_6\text{O}_{19}$  are known. Percolumbic acid ( $\text{HCbO}_4$ ) is formed by treating  $\text{HCbO}_3$  with  $\text{H}_2\text{O}_2$ .

Normal and oxyfluorides, such as  $\text{CbF}_5$  and  $\text{CbOF}_3$  are known. Salts of the type  $\text{K}_2\text{CbF}_7$  and  $\text{K}_2\text{CbOF}_5$  have been prepared. Likewise, normal and oxychlorides are known.

Tantalum forms compounds similar in composition to those of columbium.

**Commercial Manufacture.**—Columbium may be obtained by the thermit process, by the electrolysis of a solution of fluoxy-columbate, or by reduction of the chloride ( $\text{CbCl}_4$ ) with hydrogen.

Tantalum is obtained by the electrolysis of fused  $\text{K}_2\text{TaF}_6$  or of a tantalum salt in a 3 per cent solution of sulfuric acid. The metal is obtained as a powder which is purified by repeated extraction with water and acids. It is then pressed into bars, heat-treated and finally fused in a vacuum furnace.

**Uses.**—Before the introduction of tungsten, tantalum was largely used as filaments for electric lamps. It finds use at present as a substitute for platinum for making standard weights and chemical apparatus, as electrodes which are not attacked appreciably by aqua regia, and as points for steel pens. Because of its valve effect, *e. g.*, giving a pulsating direct current when connected in alternating lighting circuits, it is used in rectifiers for charging storage batteries. Certain of its alloys, such as ferrotantalum and nickel and tantalum, show promise of industrial use.

## GROUP VI

**Introduction.**—*Oxygen* and *sulfur* are the short period elements belonging to this group (VI). The former has been discussed in Chapter I. *Sulfur*, together with the elements of Division A (*selenium*, atomic weight, 78.96, and *tellurium*, atomic weight, 127.61), constitute a family in which the gradations of properties are clearly evidenced. The melting- and boiling-points, densities, and atomic volumes increase as the atomic weights become greater. These elements exist in different allotropic forms and exhibit valences of 2, 4 and 6. Sulfur is a non-metal, whereas tellurium possesses all of the physical properties of a metal. They form hydrides of the general type  $\text{RH}_2$  ( $\text{H}_2\text{O}$ ,  $\text{H}_2\text{S}$ ,  $\text{H}_2\text{Te}$ ,  $\text{H}_2\text{Se}$ ). The stability of these hydrides decreases as their molecular weights increase. The oxides of these elements correspond to the general formula  $\text{RO}_2$  and  $\text{RO}_3$  and are the anhydrides of the acids represented by  $\text{H}_2\text{RO}_3$  and  $\text{H}_2\text{RO}_4$ .

The members of Division B (Group VI) are *chromium* (Cr, atomic weight, 52.01), *molybdenum* (Mo, atomic weight, 95.95), *tungsten* (W, atomic weight, 183.92) and *uranium* (U, atomic weight, 238.07). These elements are distinctly metallic. They form oxides of which those of higher molecular weight are acidic. These oxides form series of compounds, such as the chromates, the molybdates, etc. In this respect they resemble sulfur. The metals of this group have a tendency to unite with oxygen and in such combination ( $\text{CrO}^{++}$ ,  $\text{MoO}_2^{++}$ ,  $\text{UO}_2^{++}$ ) replace the hydrogen of acids to form salts. This property increases with the atomic weight. Chromium forms two basic hydroxides,  $\text{Cr(OH)}_2$  and  $\text{Cr(OH)}_3$ , which are the parent substances of a great many chromous and chromic salts. Molybdenum and tungsten are distinctly acidic, whereas uranium is both acid- and base-forming. The similarity in the properties of successive horizontal elements in Mendeléeff's table is here particularly in evidence. For example, *vanadium*, *chromium* and *manganese* are closely related to one another by virtue of very similar physical and chemical properties. *Molybdenum* and *columbium*, and also *tungsten* and *tantalum*, exhibit close relationships.

## CHAPTER XL

### SULFUR, SELENIUM AND TELLURIUM AND THEIR COMPOUNDS

#### SULFUR

*Precipitated Sulfur*, U. S. P. XIII

*Sublimed Sulfur*, U. S. P. XIII

*Washed Sulfur*, N. F. VIII

Symbol, S. Valence, II, IV, VI. Atomic Weight, 32.066;  
Atomic Number, 16

**History and Occurrence.**—This non-metallic element has been known since remotest time. On account of its inflammable nature, the early alchemists considered it the “principle of combustibility” or phlogiston. (See p. 83.) In 1777, Lavoisier classed it among the elements.

Free sulfur is found in the volcanic regions of Sicily (provinces of Caltonisetta and Girgenti), in Chile and Peru, in the United States (Utah, Colorado, California, Nevada, Idaho, Texas and Wyoming) and, in fact, in all of the volcanic regions of the world. In Louisiana, there is a deposit more than  $\frac{1}{2}$  mile in diameter. Formerly, it was believed that such deposits were of volcanic origin, but it is now generally held that they were formed either by the deposition of sulfur from sulfur-bearing waters or by the action of organic agencies upon *gypsum* ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ). In combination, the element occurs chiefly as sulfides or sulfates. The sulfides, *e. g.*, *copper pyrites* ( $\text{CuFeS}_2$ ), *galena* ( $\text{PbS}$ ), *zinc blende* ( $\text{ZnS}$ ) and *cinnabar* ( $\text{HgS}$ ) are commercially important on account of their metals. The sulfates, *e. g.*, *gypsum* ( $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ ), *barytes* ( $\text{BaSO}_4$ ), *celestite* ( $\text{SrSO}_4$ ) and *kieserite* ( $\text{MgSO}_4 \cdot (\text{H}_2\text{O})_n$ ), are very plentiful and useful. The element occurs also in the animal and vegetable kingdom as a constituent of hair and wool, volatile oils of mustard and garlic, and in albuminous bodies. About 3,150,000 long tons (long ton 2240 lbs.) of sulfur were produced in the United States in 1941, most of it being obtained from the Louisiana deposits by a process described on p. 561.

**Physical Properties.**—Sulfur may appear in two distinct and characteristic *solid* forms, in two different *liquid* forms, and as a vapor. These allotropic modifications differ markedly from one another in physical properties. The physical properties of each allotrope are given below:

1. *Rhombic Sulfur or  $\alpha$ -Sulfur.*—When carbon disulfide is allowed to evaporate spontaneously from a solution of commercial sulfur in this solvent, rhombic crystals of sulfur are formed. These crystals have a density of 2.07 and melt at  $112.8^\circ \text{ C.}$  to form  $\text{S}\lambda$ . They

are nearly insoluble in water and in alcohol. One Gm. dissolves slowly and usually incompletely in 2 cc. of carbon disulfide. One Gm. is soluble in about 70 cc. of chloroform, in 150 cc. of ether, and in 100 cc. of olive oil. Rhombic sulfur is a very poor conductor of electricity and becomes negatively electrified on friction. It ignites in air at a temperature of 363° C., and burns with a blue flame, forming quantities of sulfur dioxide. It is stable at temperatures below 96° C. Roll sulfur and most "flowers of sulfur" are crystalline in structure and are examples of this form of the element.

2. *Monoclinic Sulfur or  $\beta$ -Sulfur.*—This form of sulfur may be obtained by partially cooling molten sulfur, piercing the crust that forms, and pouring off the still liquid portion. The interior of the vessel will be found lined with needles of this crystalline form. These needles are nearly colorless, have a density of 1.957, melt at 119.25° C. to form  $S\lambda$ , and are different from the rhombic variety in all physical respects. This form is stable above 96° C., but upon cooling it reverts to the rhombic sulfur, *e. g.*, monoclinic  $S \rightleftharpoons$  rhombic  $S$  at 96° C.

3. *Liquid Sulfur.*—When sulfur is heated above its melting-point, several interesting phenomena are observed. At approximately 160° C. a noticeable change takes place. The pale yellow, mobile liquid ( $S\lambda$ ) gradually darkens and becomes more viscous until at about 180° C. the product is dark brown in color and has reached a maximum viscosity ( $S\mu$ ). On continued heating the viscosity becomes less, until at 444.6° C. the liquid boils and sulfur vapors are evolved. When the  $\lambda$ -sulfur is allowed to slowly cool, either  $\alpha$ -sulfur or  $\beta$ -sulfur result, both of which are soluble in carbon disulfide. However, when the viscous variety is rapidly cooled or the more highly heated sulfur poured into water, an elastic substance (resembling rubber) insoluble in carbon disulfide is obtained. This variety is often called *plastic sulfur* and is considered to be a supercooled liquid. This substance becomes hard and brittle upon standing for several days and is then found to contain about 70 per cent of rhombic sulfur, soluble in carbon disulfide, and 30 per cent of another variety which is very nearly insoluble in any solvent. This latter is called *amorphous sulfur*. A. Smith and his collaborators<sup>1</sup> regard molten sulfur as a mixture of two isomers,  $S\lambda$  and  $S\mu$ , in dynamic equilibrium.  $S\lambda$  is light yellow in color and mobile, whereas  $S\mu$  is dark brown and viscous. At the lower temperatures of molten sulfur,  $S\lambda$  predominates, but as the higher temperatures are reached  $S\mu$  increases ( $S\lambda \rightleftharpoons S\mu$ ). This change from  $S\lambda$  to  $S\mu$  is reversible, as shown when sulfur at its boiling-point is allowed to cool slowly.

The physical properties of the *official* forms of sulfur may be summarized as follows:

*Precipitated Sulfur.*—This is a very fine, pale yellow, amorphous or microcrystalline powder, without odor or taste.

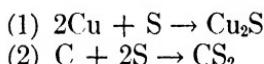
<sup>1</sup> Abstract Jour. Chem. Soc., 2, 20, 451, 757 (1907).

One Gm. is practically insoluble in water, and nearly insoluble in alcohol. One Gm. dissolves slowly and usually incompletely in about 2 cc. of carbon disulfide. One Gm. dissolves in about 100 cc. of olive oil.

*Sublimed Sulfur.*—This form is a fine, yellow, crystalline powder having a faint odor and taste. Its solubility is the same as that of Precipitated Sulfur.

*Washed Sulfur.*—This is a fine, yellow, crystalline powder, without odor or taste. Its solubility is the same as that of the other forms of sulfur. In addition the N. F. VIII notes a solubility of 1 Gm. in 150 cc. of ether.

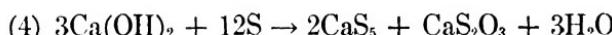
**Chemical Properties.**—Under reduced pressure and at low temperatures, the formula of sulfur vapor is  $S_8$ . The freezing-point depressions of solutions of sulfur also indicate  $S_8$ . At  $1000^{\circ}\text{ C.}$ , however, the formula is  $S_2$ . Sulfur is a very active element. It unites with most metals (1) and non-metals (2) to form sulfides. When sulfur is treated with oxidizing agents in the presence of water, sulfuric acid is formed. (See Sulfuric Acid, p. 136.)



When sulfur is oxidized with oxygen (burned), it evolves suffocating fumes of sulfur dioxide (3).



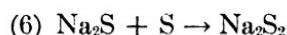
When boiled with a solution of calcium hydroxide, sulfur is dissolved with the formation of calcium thiosulfate and calcium penta-sulfide (4). It can easily be precipitated from such a solution by acidification. (See Preparation of Precipitated Sulfur, p. 562.)



Its solubility in calcium hydroxide is very similar to its solubility in hot solutions of the alkali hydroxides, *e. g.*, sodium hydroxide (5).



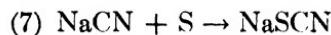
Part of its solubility in alkali hydroxides is probably due to the fact that it is also soluble in solutions of alkali sulfides such as sodium sulfide (6). Thus, it is reasonable to expect that the reaction does not contain only the products shown in equation (5) but also sulfides of sodium containing more sulfur such as are shown in equation (6).



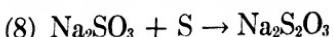
or



Sulfur reacts readily with the alkali cyanides (7) to form thiocyanates.



Finally, sulfur reacts with sulfites to form thiosulfates (8).



**Commercial Production of Sulfur.**—The recovery of sulfur from mixtures with limestone, clay, gypsum, etc., depends upon the liquefaction of the sulfur either by its own heat of combustion or by heat from other sources. In Sicily, sulfur is recovered in a crude furnace called a "calcarone." These "calcarones" are semicircular, stone-walled pits, 35 feet in diameter and 10 feet deep, dug into the side of a hill. As the quarried sulfur rock is packed in the calcarone, vertical air-passages are constructed by means of which the temperature of the crude furnace is regulated (Fig. 22). The kilns are fired from the top and the heat generated by burning some of the sulfur is sufficient to liquefy the remainder. The molten sulfur is drawn off at the base of the furnace into square stone receptacles from which it is ladled into damp poplar wood moulds. The truncated cones of sulfur thus produced weigh from 100 to 130 pounds. On account of the amount of sulfur consumed by



FIG. 22.—A calcarone. (From Molinari, General and Industrial Chemistry, courtesy of the Blakiston Company.)

combustion, the yield is approximately 50 per cent. Because of the destruction of crops by the immense volume of sulfur dioxide evolved, these calcarones are rigidly restricted to certain areas. Other methods (Gill, Gritti, Orlando) of liquefying sulfur are also in use.

The sulfur obtained from these various kilns contains about 3 per cent of earthy material and must be refined to meet the commercial requirements. The refinery consists of a large stone chamber with a safety valve. This valve is usually located in the roof and is designed to take care of any developed pressure. The molten sulfur is contained in iron retorts (usually two) which communicate with the chamber. When the sulfur vapors first enter the stone chamber, they ignite and convert the air into nitrogen and sulfur dioxide. The next vapor diffuses through a mass of relatively cold gas and condenses on the walls and floors of the chamber in a fine crystalline form called *flowers of sulfur*. By conducting the sublimation so as not to raise the temperature of the condensing chamber, all of the sulfur may be converted to this form. If "roll sulfur" is desired,

the rate of sublimation is increased. When the sulfur condenses in the chamber, it is immediately melted to a liquid which is run off from the bottom of the condenser and cast in moulds.

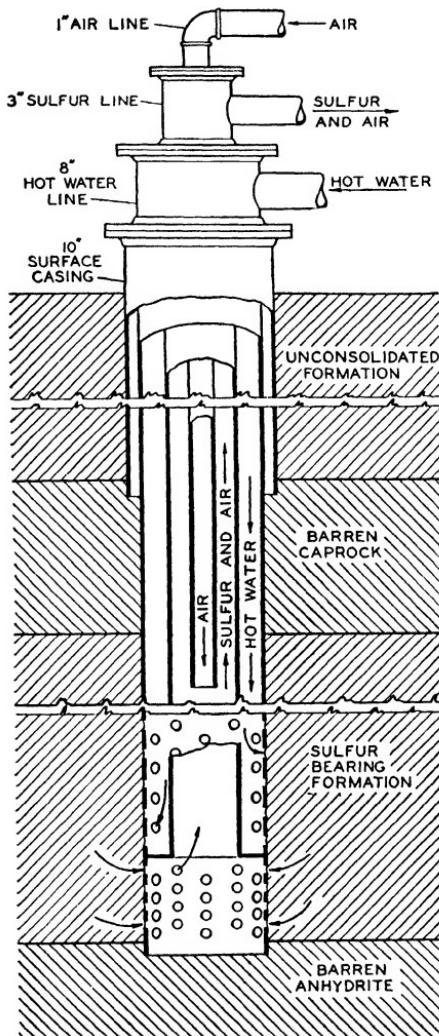


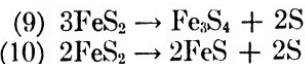
FIG. 23.—Sulfur Well. (By permission from *Inorganic Chemical Technology*, by Badger and Baker, copyrighted, 1941, by McGraw-Hill Book Company, Inc.)

The Louisiana deposits are worked by a process that was devised by Herman Frasch in 1891.<sup>1</sup> A bore-hole is sunk some 700 to 1000 feet through clay, quicksand and rock until the sulfur bed is reached. Three concentric pipes of 8, 3 and 1 inch in diameter are then lowered into the hole. (See Fig. 23.) Superheated water (180° C.) is pumped down the outer pipe to the sulfur bed. When

<sup>1</sup> J. Chem. Education, 6, 129 (1929).

the sulfur is melted, compressed air is forced down the 1-inch pipe. The molten sulfur mixes with the air, its specific gravity is lowered and it then rises in the 3-inch tube and flows out above ground into large wooden enclosures in which it solidifies. This sulfur is about 98 per cent pure.

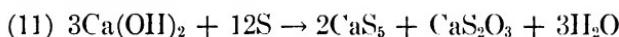
Sulfur may be obtained by heating sulfide ores, *e. g.*, iron pyrites, in closed retorts (9 or 10).



The U. S. Pharmacopœia XIII recognizes two forms of sulfur, *viz.*, Sublimed Sulfur and Precipitated Sulfur. Washed Sulfur is recognized by N. F. VIII. Each one of these official forms of sulfur, when dried for eighteen hours over sulfuric acid, must contain not less than 99.5 per cent of sulfur.

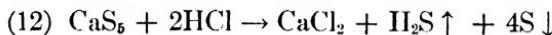
1. *Sublimed Sulfur*.—Sublimed Sulfur or "flowers of sulfur" is made by the process previously described on p. 560.

2. *Precipitated Sulfur*.—Precipitated Sulfur is a very fine amorphous or microcrystalline powder having a pale yellow color and no odor or taste. It is more readily and completely soluble in carbon disulfide than either flowers of sulfur or washed sulfur. It is prepared by boiling together sublimed sulfur and milk of lime for one hour. During the operation both calcium pentasulfide and thiosulfate are formed (11).



The mixture is filtered and diluted hydrochloric acid added with constant stirring until the liquid is *nearly* neutralized but still retains an alkaline reaction to red litmus. The precipitated sulfur is collected on a strainer and washed with water until the washings are neutral to litmus and give no test for calcium with ammonium oxalate test solution. The product is then dried rapidly.

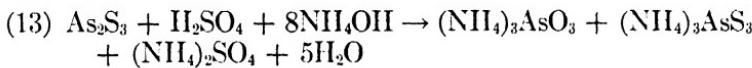
It will be noted that during the precipitation of the sulfur (12),



the liquid is kept alkaline and the addition of diluted hydrochloric acid is discontinued while the liquid is still alkaline to litmus. Although giving a lesser yield of precipitated sulfur than would be obtained if the liquid was made slightly acid, this is done for several excellent reasons. Most sublimed sulfur contains a small amount of arsenic as the trisulfide, and when this is digested with hot milk of lime, calcium sulfarsenite  $[\text{Ca}_3(\text{AsS}_3)_2]$  is formed. This is soluble in the alkaline liquid. However, if the liquid is made acid by the addition of hydrochloric acid, the calcium sulfarsenite is decomposed into the insoluble arsenic trisulfide which will again contaminate the precipitated sulfur. It is quite evident that the sulfides of calcium are very much more readily decomposed by hydrochloric acid than is calcium thiosulfate, the latter not being

materially affected until all of the sulfides have been acted upon and only when the liquid is decidedly acid to litmus. Any sulfur precipitated by the decomposition of calcium thiosulfate is not only much coarser than that obtained from the sulfides but it is also insoluble in carbon disulfide; qualities that are most undesirable in precipitated sulfur.

*3. Washed Sulfur.*—Washed Sulfur is a fine, yellow powder having a faint odor and taste. Nearly all sublimed sulfur contains impurities of arsenic, as the trisulfide ( $\text{As}_2\text{S}_3$ ), traces of selenium and sulfuric acid, formed by the oxidation of the sulfur and the subsequent hydrolysis of the trioxide. These impurities may be removed by passing the sublimed sulfur through a No. 30 sieve and macerating the uniform fine powder in approximately a 1 per cent solution of ammonia for three days. The sulfur is then transferred to a strainer and washed with water until the washings do not impart a blue color to red litmus paper. The product is allowed to drain and then is dried rapidly at a moderate heat. Lastly, it is passed through a No. 30 sieve. By this process the arsenic is removed as soluble ammonium arsenite or sulfarsenite (13), the selenium is likewise converted to soluble ammonium compounds, and the sulfuric acid is changed to ammonium sulfate (13).



Washed Sulfur, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of S.

**Laboratory Preparation of Precipitated Sulfur.**—Slake 12.5 Gm. of Lime (N. F. VIII) and thoroughly mix it with 125 cc. of water. Add 25 Gm. of flowers of sulfur, previously sifted and, after thoroughly mixing, add 250 cc. of water and boil the mixture in a porcelain or glass vessel during one hour. The mixture should be stirred frequently and the water lost by evaporation replaced. Now cover the vessel and allow it to stand until the contents are cool and the supernatant liquid becomes clear. Carefully draw off the clear solution and filter the remainder. To the combined liquids gradually add hydrochloric acid, previously diluted with an equal volume of water, until the liquid is nearly neutralized but still retains an alkaline reaction and a yellow color. The solution should be stirred constantly during the addition of the acid. Collect the precipitate on a strainer and wash it until the washings are neutral to litmus paper and do not give a test for calcium with ammonium oxalate test solution. Then dry the product rapidly.

**Pharmacological Action of Sulfur.**—Sulfur has been used therapeutically since antiquity and during that time, certain well-defined uses have emerged. These are (1) cathartic action, (2) parasiticide in scabies, (3) stimulant in alopecia, (4) fumigation, and (5) miscellaneous skin diseases.

1. Sulfur exerts a mild cathartic (aperient) effect and therefore is used to soften the stools, particularly when the patient has

hemorrhoids. The classical effect of "sulfur and molasses" is based largely on this action. The reason that it acts as a cathartic is because the sulfur reacts with protein to liberate, among other things, hydrogen sulfide which is mildly irritant to the intestinal tract. This action is very gradual, unless a finely divided form of sulfur, such as Precipitated Sulfur, is used. "Washed Sulfur" is preferred for producing this effect.

2. Although sulfur is an insoluble and practically inert substance by itself, it has been shown that in contact with living tissue it forms hydrogen sulfide and an oxidation product, pentathionic acid, both of which have been shown experimentally to be germicidal and fungicidal. These products of interaction between sulfur and living tissue are responsible for the effectiveness of sulfur in the treatment of various skin conditions caused by fungus infections and parasites. For this type of action the sulfur should be in as finely a divided state as possible, which makes "precipitated sulfur" the one of choice. In the form of an ointment or as free sulfur, sulfur has been used a great deal for the treatment of scabies (itch). A novel method of administration is with the "sulfur foam" applicator in which the finely divided sulfur is applied to the skin as a soapy foam and allowed to dry. Since the itch mite eggs are not affected by sulfur, repeated application is necessary (usually for three successive days) to kill both the grown mites and the mites which hatch out. It is of utmost importance to prevent reinfection by wearing clean clothes and changing bedclothing. Other medications, *e. g.*, benzyl benzoate, have largely superseded sulfur for this type of therapy.

3. Because sulfur also has a local stimulant and keratolytic action on the skin, it helps to overcome congestion and to soften horny elements and scaly formations. For this reason it has been used in the treatment of seborrheic alopecia (baldness). In the form of an ointment, it is applied to the scalp.

4. Because of the fact that sulfur forms sulfur dioxide when burned, it has been used for fumigating. Its use in this capacity has not proved too successful, but it has proven to be quite an effective insecticide for bedbugs, roaches, mosquitoes, etc. The procedure is to burn 2 to 3 pounds of sulfur per 1000 cubic feet of room space. Sulfur for this purpose is usually supplied in  $\frac{1}{4}$  and 1 pound cakes, usually with a wick in the middle of the "candle." The sulfur cake should be placed on some non-inflammable object so that the floor does not burn. It works best when the air is saturated with moisture, but at the same time it is well to remember that under these conditions sulfur dioxide is an effective bleaching agent. Therefore, objects that might be bleached should be removed from the room.

5. Because of its keratolytic and fungicidal action, sulfur has been used for a multiplicity of skin diseases such as psoriasis, acne, etc.

**Pharmaceutical Preparations and Uses.**—1. *Precipitated Sulfur* (Sulfur *Præcipitatum*), U. S. P. XIII.—Precipitated Sulfur, when

dried for eighteen hours over sulfuric acid, contains not less than 99.5 per cent of S. This form of sulfur is also known as "lac sulfur" or "milk sulfur," these names being derived from the fact that formerly the precipitated sulfur of commerce was made by using sulfuric acid as a precipitant rather than hydrochloric acid. This resulted in a deposit of calcium sulfate in the sulfur and imparted an almost white color to it. This form of sulfur is used largely for external application. Because of its fine state of subdivision, it should be used in ointments. Average dose—4 Gm. (approximately 60 grains).

2. *Sublimed Sulfur* (*Sulfur Sublimatum, Flowers of Sulfur*), U. S. P. XIII.—Sublimed Sulfur, when dried over sulfuric acid for eighteen hours, contains not less than 99.5 per cent of S. This form of sulfur is sometimes used internally, although the preferable form is Washed Sulfur. It is also used externally in ointment form.

3. *Washed Sulfur* (*Sulfur Lotum*), N. F. VIII.—"Washed Sulfur, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of S." It is prepared as indicated on p. 563. It is the preferable form for internal administration. Average dose—4 Gm. (approximately 60 grains).

4. *Sulfurated Lime Solution* (*Liquor Calcis Sulfuratæ, Vleminckx' Solution, Vleminckx' Lotion*), N. F. VIII.—(See p. 336.) This preparation is used in acne, etc., for the characteristic effect of sulfides.

5. *Compound Senna Powder* (*Pulvis Sennæ Compositus, Compound Licorice Powder*), N. F. VIII.—This is a preparation containing 8 per cent of washed sulfur together with 18 per cent senna, 23.6 per cent glycyrrhiza, a small quantity of fennel oil and the remainder sucrose. It is used as a mild cathartic. Average dose—4 Gm. (approximately 1 drachm).

6. *Alkaline Sulfur Ointment* (*Unguentum Sulfuris Alkalinum*), N. F. VIII.—(See p. 237.) This preparation contains 20 per cent of sublimed sulfur which is mixed with 10 per cent of potassium carbonate and 5 per cent water. This mixture is incorporated into a base composed of wool fat, petrolatum and yellow wax. It is used in the treatment of scabies, etc.

7. *Compound Sulfur Ointment* (*Unguentum Sulfuris Compositum, Wilkinson's Ointment, Hebra's Itch Ointment*), N. F. VIII.—(See p. 320.) This ointment contains precipitated calcium carbonate (10 per cent) and sublimed sulfur (15 per cent) which are incorporated into an ointment base containing juniper tar, soft soap and solid petroxolin. It is used in the treatment of scabies, etc.

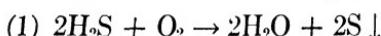
## SULFUR COMPOUNDS

**Hydrides.**—**Hydrogen Sulfide** (*Sulfuretted Hydrogen, Hydrosulfuric Acid*),  $H_2S$ .—This compound was first examined by C. Scheele.

**Occurrence.**—In Nature, hydrogen sulfide is found in volcanic vapors and many mineral waters contain small quantities of it.

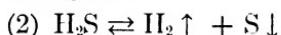
(See p. 49.) It is always one of the products that results from the putrefaction of organic sulfur-bearing materials. For example, "sewer gas" is composed of ammonia, methane, carbon dioxide and from 1 to 10 per cent of hydrogen sulfide. Small quantities of this gas are produced during intestinal putrefaction.

*Physical Properties.*—Hydrogen sulfide is a colorless gas having an offensive odor (rotten eggs) and a sweetish taste. It is slightly heavier than air (density, 1.18; air = 1). One volume of water dissolves 4.37 volumes of hydrogen sulfide at 0° C. (760 mm.) and 2.609 volumes of the gas at 25° C. (760 mm.). Its aqueous solutions are feebly acid to litmus and when exposed to air decompose into free sulfur and water (1).

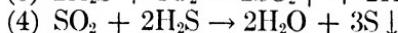
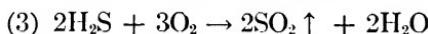


Under a pressure of about 17 atmospheres, the gas is converted to a colorless liquid which has a density of 0.96 at -60° C. and a boiling-point of -61.8° C. The liquid solidifies at -82.9° C.

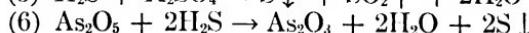
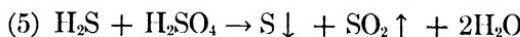
*Chemical Properties.*—Heat and light decompose hydrogen sulfide into its constituent elements (2). At high temperatures (about 500° C.) the decomposition is complete. The decomposition of hydrogen sulfide in aqueous solutions (1) is accelerated by light, hence its solutions should be kept in well-closed containers in a cool dark place.



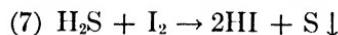
Hydrogen sulfide burns in air with a pale blue flame (3). The sulfur dioxide is sometimes reduced to free sulfur (4).



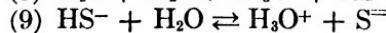
Hydrogen sulfide is an active reducing agent. For example, sulfuric acid is reduced to sulfur dioxide and sulfur (5), and arsenic pentoxide is converted into arsenic trioxide (6).



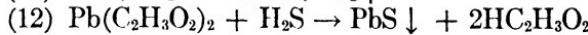
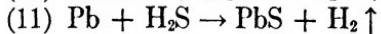
Chlorine, bromine and iodine displace the sulfur of hydrogen sulfide to form the hydrogen halides and sulfur is precipitated (7).



When hydrogen sulfide is dissolved in water, *hydrosulfuric acid* is formed. This dibasic acid dissociates into hydrosulfide ions (8) which, in turn, are only slightly dissociated into sulfide ions (9). The fact that at 18° C. only 0.07 per cent of H<sub>2</sub>S in tenth-normal solution is dissociated into HS<sup>-</sup> accounts for the "weakness" of this acid. The percentage dissociation of the HS<sup>-</sup> into S<sup>2-</sup> is even less than that of water and, therefore, is practically negligible.



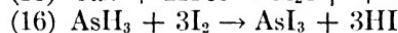
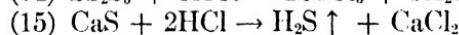
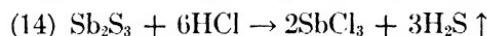
Hydrosulfuric acid reacts with bases to form salts (sulfides) (10). Its hydrogen is displaced by metals (11). The acid enters into double decomposition reactions with salts such as lead acetate, zinc sulfate, etc. (12).



*Methods of Preparation.*—(a) Hydrogen sulfide may be prepared by passing hydrogen through boiling sulfur (13). Combination takes place between 200° C. and 358° C. and is practically complete at 310° C. This method is economically impractical from a laboratory or commercial standpoint.



(b) The gas is usually prepared by the action of diluted sulfuric or hydrochloric acids upon metallic sulfides. Because of its availability and cheapness, ferrous sulfide is generally used. A concentrated sulfuric acid should not be used in this reaction because not only will the acid be reduced to sulfur dioxide (5), which will contaminate the gas, but also an anhydrous ferrous sulfate will coat the iron sulfide and stop any further reaction. Although the hydrogen sulfide obtained in this manner is washed with water, it still will be contaminated with many impurities, such as hydrogen, arsine, etc. The former results from the action of the acid upon free iron present in the ferrous sulfide, whereas, the latter is occasioned by the reducing action of hydrogen upon compounds of arsenic which are nearly always present in commercial grades of ferrous sulfide. A hydrogen sulfide that is freed from hydrogen may be obtained by allowing hydrochloric acid to act upon antimony or calcium sulfides (14) (15). Hydrogen sulfide may be freed from arsine by first drying the gas and then passing it over powdered iodine (16).

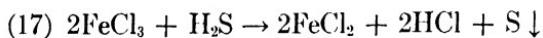


*Detection.*—Hydrogen sulfide may be detected by its characteristic obnoxious odor. It should be remembered that there is only a slight difference in the odor of a harmless concentration of the gas and that of a lethal one.

*Pharmacological Action.*—Hydrogen sulfide is a great deal more toxic than is generally realized. In fact, it closely approaches hydrogen cyanide in toxicity. A concentration of 1 part in 10,000 of air produces conjunctivitis and prolonged exposure may also cause an irritation of the entire respiratory tract followed by edema. Lethal concentrations (15 to 20 parts in 10,000) produce death by direct paralysis of the respiratory center. *In vitro*, hemoglobin is reduced by hydrogen sulfide to sulfhemoglobin, which is a stable brown or brownish-green compound, considered to be the cause of

the discoloration of cadavers. Cases of acute poisoning may be treated by using artificial respiration together with inhalations of oxygen containing 5 per cent of carbon dioxide.

*Pharmaceutical Preparations and Uses.*—The U. S. Pharmacopœia XIII recognizes a test solution of this gas. It is described as being a saturated aqueous solution of hydrogen sulfide made by passing H<sub>2</sub>S into cold distilled water. The Pharmacopœia directs that the solution be kept in small amber colored bottles, filled nearly to the top and preserved in a cool, dark place. The test solution should have a strong odor of hydrogen sulfide and, when added to an equal volume of ferric chloride test solution, it should produce a heavy precipitate of sulfur (17).

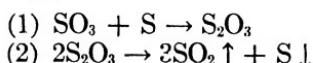


Hydrogen sulfide is used for precipitating certain cations, such as As<sup>+++</sup>, Sb<sup>+++</sup>, Sn<sup>++</sup>, Hg<sup>++</sup>, Bi<sup>+++</sup>, Cu<sup>++</sup>, Cd<sup>++</sup>, etc., from acid solution. Ammonium sulfide (prepared by saturating ammonium hydroxide with hydrogen sulfide) also precipitates another group of cations (Fe<sup>+++</sup>, Ni<sup>++</sup>, Co<sup>++</sup>, Mn<sup>++</sup>).

**Hydrogen Polysulfides.**—*Hydrogen disulfide* (H<sub>2</sub>S<sub>2</sub>), *hydrogen tri-sulfide* (H<sub>2</sub>S<sub>3</sub>) and *hydrogen pentasulfide* (H<sub>2</sub>S<sub>5</sub>) are known. They may be prepared by adding a cold solution of the alkali or alkaline earth polysulfides to a cold concentrated hydrochloric acid. The polysulfides of hydrogen have a sharp unpleasant taste and an odor similar to that of hydrogen sulfide. They readily decompose into hydrogen sulfide and sulfur. H<sub>2</sub>S<sub>2</sub> is a liquid having a specific gravity of 1.376 at 20° C. It may be converted into a solid having a melting-point of -88° C. H<sub>2</sub>S<sub>3</sub> is also a liquid having a specific gravity of 1.496 at 15° C. In the solid state it melts at -53° C. H<sub>2</sub>S<sub>5</sub> is a liquid having a specific gravity of 1.71 at 15° C.

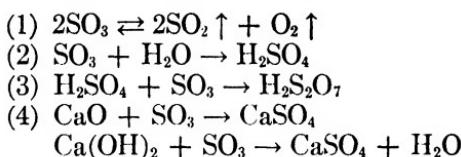
**Oxides.**—Four oxides of sulfur are known, *viz.*, the *sesquioxide* (S<sub>2</sub>O<sub>3</sub>), *sulfur trioxide* (SO<sub>3</sub>), *sulfur dioxide* (SO<sub>2</sub>) and *sulfur heptoxide* (S<sub>2</sub>O<sub>7</sub>).

**Sulfur Sesquioxide** (S<sub>2</sub>O<sub>3</sub>).—Sulfur sesquioxide is a bluish-green, crystalline solid formed by carefully adding sulfur to sulfur trioxide (1). When this oxide is warmed, it readily decomposes into SO<sub>2</sub> and S (2).

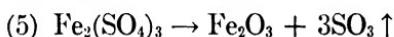


**Sulfur Trioxide** (SO<sub>3</sub>).—Sulfur trioxide was mentioned by Basil Valentine in the fifteenth century. It was first obtained by N. Lemery, in 1675, by distilling green vitriol. It is a colorless liquid having a specific gravity of 1.923 at 20° C. When the liquid is kept at 16° C., it slowly crystallizes in long transparent prisms having a melting-point of 16.83° C. When the liquid is allowed to crystallize at ordinary temperatures, crystalline fibers melting at 40° C. are formed. Therefore, it would appear that sulfur trioxide exists in two modifications.

*Chemical Properties.*—When sulfur trioxide is heated, it decomposes into sulfur dioxide and oxygen (1). It combines with water to form sulfuric acid, of which it is the anhydride (2). The combination is accompanied by an evolution of a large quantity of heat. Sulfur trioxide dissolves in concentrated sulfuric acid to form a series of compounds of which *oleum* or *fuming sulfuric acid* is an example (3). Under the heading of Reagents, the U. S. Pharmacopœia XIII describes fuming sulfuric acid as being a heavy, fuming, colorless, oily liquid containing at least 84 per cent of total SO<sub>3</sub>, corresponding to about 15 per cent of free SO<sub>3</sub>. It should have a density of about 1.87 and, upon ignition, should not yield over 0.02 per cent of residue. It combines directly with a number of oxides and hydroxides to form the corresponding salts (4), and it frequently acts as an energetic oxidizing agent.



*Methods of Preparation.*—Sulfur trioxide may be obtained by distilling ferric sulfate (5).



Sulfur dioxide and oxygen slowly and incompletely combine to form sulfur trioxide (6). In 1875, C. Winkler effected a more complete combination by passing the gases over platinized asbestos heated to about 400°C. The best conditions for this reaction have been carefully studied, and as a result we have the so-called *contact process* for the commercial manufacture of sulfuric acid (*q. v.*).

It has been ascertained that with a gas mixture containing 7 per cent of SO<sub>2</sub>, 10 per cent of oxygen and 83 per cent of nitrogen, a yield of SO<sub>3</sub> equal to 99 per cent of the theoretical may be obtained by bringing the gases in contact with finely divided platinum heated to 434°C. The yields are less for temperatures above and below 434°C. Finely divided and heated oxides of some other metals (Fe<sub>2</sub>O<sub>3</sub>, MnO<sub>2</sub>, etc.) will also catalyze this reaction.



*Uses.*—When perfectly dry, this oxide of sulfur possesses no caustic properties. However, traces of moisture produce sulfuric acid which destroys organic matter. It is used in the manufacture of sulfuric acid and various dyes, *e. g.*, alizarin, indigo, etc.

**Sulfur Dioxide** (SO<sub>2</sub>) and **Sulfurous Acid** (H<sub>2</sub>SO<sub>3</sub>).—This oxide of sulfur is present in volcanic gases and in the spring waters of volcanic areas. Coal smoke contains appreciable quantities of sulfur dioxide, and hence the atmosphere of large cities is contaminated with it. In 1775, J. Priestley obtained the pure gas and claimed

it to be a definite compound. Later A. L. Lavoisier determined its composition.

*Physical Properties.*—Sulfur dioxide is a colorless gas possessing a characteristic pungent and irritating odor. It has a density of 2.264 (air = 1). One volume of water at 0° C. (760 mm.) dissolves nearly 80 volumes of gas and at 25° C. (760 mm.) 32.8 volumes. The gas dissolves in alcohol and yields about a 26.5 per cent solution. The dry gas is neutral in reaction but its aqueous solutions are acid to litmus. The critical temperature is 157.2° C. and the critical pressure about 78 atmospheres. The gas is easily liquefied to a colorless liquid which boils at -10° C. This liquid is an excellent solvent for iodine, phosphorus and sulfur. Some inorganic salts dissolve in it to form addition products, such as  $KI \cdot 4SO_2$ ,  $KI \cdot 4I \cdot SO_2$ , etc. The rapid evaporation of liquid sulfur dioxide converts it into a white solid melting at -72.7° C.

*Chemical Properties.*—Sulfur dioxide is stable even at high temperatures. It does not burn or support combustion. Under the influence of a catalyst, it unites with oxygen to form sulfur trioxide. In the presence of camphor (catalyst) or in direct sunlight,  $SO_2$  forms addition compounds with chlorine (1) and fluorine (2). Sulfur dioxide forms a hydrate containing 7 molecules of water ( $SO_2 \cdot 7H_2O$ ). This may be obtained by cooling a saturated aqueous solution of the gas. Sulfur dioxide is a good reducing agent. For example, if it is passed into an aqueous solution of iodine, sulfuric and hydriodic acids are formed (3). In this case, the iodine is reduced (gains 2 electrons), whereas the sulfur of the sulfur dioxide is oxidized (loses 2 electrons). Sulfur dioxide also reduces permanganates to manganous salts (4), iodates to iodine (5), etc.

- (1)  $SO_2 + Cl_2 \rightarrow SO_2Cl_2$  (sulfuryl chloride)
- (2)  $SO_2 + F_2 \rightarrow SO_2F_2$  (sulfuryl fluoride)
- (3)  $I_2 + 2H_2O + SO_2 \rightarrow H_2SO_4 + 2HI$
- (4)  $2KMnO_4 + 2H_2O + 5SO_2 \rightarrow K_2SO_4 + 2MnSO_4 + 2H_2SO_4$
- (5)  $2KIO_3 + 4H_2O + 5SO_2 \rightarrow 2KHSO_4 + I_2 + 3H_2SO_4$

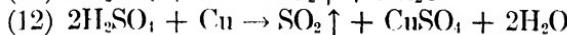
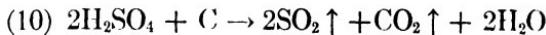
*Preparation.*—Sulfur dioxide is produced when sulfur is burned in air or oxygen (6). A very small quantity of sulfur trioxide is also formed.



The gas is usually prepared for industrial purposes by roasting metallic sulfides (7) (8) (9). This roasting process is preliminary to the recovery of certain metals from their sulfide ores. (See Copper, p. 281, and Zinc, p. 372.)

- (7)  $Cu_2S + 2O_2 \rightarrow 2CuO + SO_2 \uparrow$
- (8)  $2ZnS + 3O_2 \rightarrow 2ZnO + 2SO_2 \uparrow$
- (9)  $4FeS_2 + 11O_2 \rightarrow 2Fe_2O_3 + 8SO_2 \uparrow$

It may be obtained by reducing concentrated sulfuric acid with carbon (10), sulfur (11), or metals (12).



Sulfur dioxide is formed when sulfites are decomposed with dilute acids (13).



*Detection of Sulfur Dioxide.*—1. Sulfur dioxide may be detected by its characteristic acrid odor.

2. When a piece of paper moistened with a solution of potassium iodate and starch test solution is exposed to the gas, the starch turns blue, due to liberated iodine (5). Continued exposure of the paper to the gas will cause the blue color to disappear (3).

3. When moistened mercurous nitrate paper comes in contact with sulfur dioxide, it turns black due to the reduction of the mercurous nitrate to metallic mercury (14).

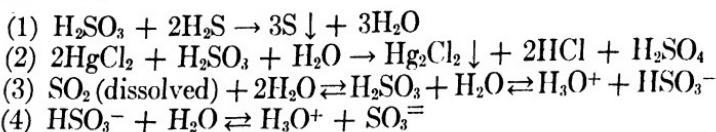


*Uses.*—Sulfur dioxide is too strong a reducing agent to be used either in or upon the body. Very dilute concentrations of the gas in air have been used with variable results in the treatment of colds. (See also Chlorine, p. 86.) It finds extensive industrial use for bleaching wool, straw and wood pulp; for fumigating; for arresting fermentation, and in the manufacture of sugar. Its principal use is in the manufacture of sulfuric acid.

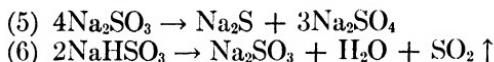
**Sulfurous Acid ( $\text{H}_2\text{SO}_3$ ).**—Despite the facts that this compound has never been isolated and that a solution of  $\text{SO}_2$  in water has every appearance of being a simple solution of gas in water, there is ample evidence that sulfurous acid actually does exist as such in solution.

*Properties.*—A saturated solution of sulfur dioxide in water is a colorless liquid having a strong odor of  $\text{SO}_2$ . It has a specific gravity of about 1.028 at 25° C. and contains between 6 and 7 per cent by weight of  $\text{SO}_2$ . It is acid in reaction and possesses strong reducing properties (1). With several compounds that are easily oxidized, it acts as an oxidizing agent (2). Being a dibasic acid, it forms both normal and hydrogen salts with bases. Aqueous solutions of normal sulfites are feebly alkaline in reaction, whereas, solutions of the hydrogen sulfites are slightly acid. Apparently, there are several equilibria existing in a solution of sulfur dioxide in water. Undoubtedly, the liquid contains a large amount of the  $\text{SO}_2$  in simple solution in the water. However, some of the  $\text{SO}_2$  combines with some of the water to form undissociated sulfurous acid. The ionization of this acid is very slight (8 per cent in tenth-normal solution), but nevertheless gives rise to hydronium ions and

the hydrosulfite ions (3). The dissociation of the latter ions into more hydronium ions and sulfite ions is even less than the primary ionization (4).



Both the normal and hydrogen salts of sulfurous acid are decomposed by heat. The former yields the sulfate and sulfide (5), whereas sulfur dioxide, water and normal sulfite are the products of the decomposition of the latter (6).



Solutions of sulfurous acid and sulfites are readily oxidized even by the air to sulfuric acid and sulfates, respectively.

*Preparations and Uses.*—An aqueous solution of sulfur dioxide is listed among the Reagents in the U. S. Pharmacopœia XIII. It should not contain more than 0.5 parts of As in 1,000,000 of the solution.

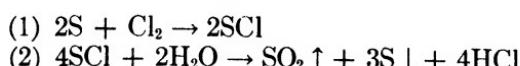
Sulfurous acid is used as a reducing agent and as a preservative. It is often used as an "antichlor" because of its property of converting chlorine into hydrochloric acid (7). Sulfites are a convenient source of SO<sub>2</sub> for laboratory purposes. Calcium hydrogen sulfite (Ca[HSO<sub>3</sub>]<sub>2</sub>) is used as a lignin solvent and bleach in the paper making industry.



**Other Sulfur Acids.**—There are a number of other thio (sulfur) acids which exist either as free acids or in the form of their salts. Their names and formulæ are given below:

Thiosulfuric acid, H <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	Peroxydisulfuric or Per-
Hyposulfurous acid, H <sub>2</sub> S <sub>2</sub> O <sub>4</sub>	sulfuric acid, H <sub>2</sub> S <sub>2</sub> O <sub>8</sub>
Permonosulfuric or Caro's acid, H <sub>2</sub> SO <sub>5</sub>	Trithionic acid, H <sub>2</sub> S <sub>3</sub> O <sub>6</sub>
Dithionic acid, H <sub>2</sub> S <sub>2</sub> O <sub>6</sub>	Tetrathionic acid, H <sub>2</sub> S <sub>4</sub> O <sub>6</sub>
	Pentathionic acid, H <sub>2</sub> S <sub>5</sub> O <sub>6</sub>

**Halogen Compounds.**—**Sulfur Monochloride** (S<sub>2</sub>Cl).—Sulfur monochloride is a light amber to yellowish-red liquid having a specific gravity of 1.678 at 20° C. It boils at 138° C. and may be converted to a solid which melts at -80° C. It is made by passing dry chlorine over melted sulfur (1). Water decomposes this compound into sulfur dioxide, free sulfur and hydrochloric acid (2). Alcohol and ether also decompose it. It is soluble in carbon disulfide.



Sulfur monochloride is an excellent solvent for sulfur. A thick, syrupy solution of about 65 per cent of sulfur in the monochloride is used in vulcanizing rubber. It is used also in the manufacture of sulfur dyes and insecticides, in dyeing textiles, and for making  $\beta\beta'$ -dichlordiethyl sulfide ('Mustard Gas').

**Sulfur Dichloride** ( $SCl_2$ ).—This unstable dark red liquid has a specific gravity of 1.621 at  $15^\circ C$ . It may be converted to a solid that melts at  $-78^\circ C$ . It is made by passing dry chlorine into sulfur monochloride at  $0^\circ C$ . Water decomposes it into the monochloride and free chlorine.

**Sulfur Tetrachloride** ( $SCl_4$ ).—This compound is stable only below  $0^\circ C$ . It is a white powder melting at  $-30^\circ C$ . It is made by passing dry chlorine into sulfur dichloride at  $-75^\circ C$ .

**Sulfur Bromide** ( $SBr$ ).—This is a heavy red liquid having a specific gravity of 2.635 at  $20^\circ C$ . It is prepared by treating sulfur with an excess of bromine and then driving off the excess of the latter with carbon dioxide. This liquid slowly decomposes into its constituent elements at its boiling-point of  $54^\circ C$ . It can be converted into a solid melting at  $-46^\circ C$ .

**Sulfur Iodides**.—Sulfur and iodine combine to form a monoiodide ( $SI$ ) and a hexiodide ( $SI_6$ ).

## SELENIUM AND TELLURIUM

Symbols, Se and Te. Valences, II, IV, VI. Atomic Weight: Se, 78.96; Te, 127.61; Atomic Number: Se, 34; Te, 52

**History.**—Berzelius (1817) discovered a new element which he called selenium (Gr. selene = "moon"), because of its close chemical relationship to tellurium (L. tellus = "earth"), discovered by Reichenstein in 1782 and named by Klaproth in 1798. Selenium was first obtained by its discoverer in the slime at the bottom of lead chambers used for making sulfuric acid.

**Occurrence.**—A small amount of tellurium occurs native. It is usually found in combination with silver, gold, lead and bismuth. Considerable amounts could be recovered during the refining of these metals and also of copper.

Selenium, on the other hand, is usually associated with sulfur and the sulfide ores. In the form of the selenides it may be recovered from the flue dust of pyrite burners and also in the electrolytic refining of copper (*q. v.*).

**Properties.**—Like sulfur, selenium and tellurium have the property of existing in different forms or allotropic modifications. A red, monoclinic, crystalline form of selenium having a density of 4.47 and a melting-point between  $170^\circ$  and  $180^\circ C$ . may be prepared. When this variety is heated between  $200^\circ$  and  $230^\circ C$  for some time, it changes into the gray variety of metallic selenium having a density of 4.8. The electrical conductivity of this form especially is very small in the dark or at ordinary temperatures but increases

markedly when exposed to light or elevations in temperature. This property is the basis for the action of the very sensitive selenium photoelectric cell. Selenium is used also in making red glass and in the rubber industry. The allotropism of tellurium is the lesser marked of the two elements, but it does occur in different forms. The fused element is metallic in appearance and has a density of 6.2. It is a good conductor of electricity. A small quantity is used in the ceramic industry.

**Pharmacological Actions of Selenium and Tellurium Ions.**—The actions of selenium, selenate, and selenite ions closely resemble those of arsenic and tellurium. The oral administration of large doses of selenium salts produces intestinal irritation and paralysis of the small blood vessels and blood-forming organs. Selenium compounds were suggested by Wassermann as being specific for tumors and cancers. It has been shown that non-toxic doses will not destroy cancer cells.

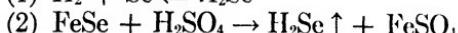
Tellurium, like selenium, resembles arsenic in its action. Because of the ease and rapidity with which tellurium compounds are reduced to the metallic state, they are relatively non-toxic.

Toxic doses produce paralysis of the blood vessels and also marked changes in the blood-forming organs. Tellurium salts acts as anti-diaphoretics and sodium tellurate has been used to suppress the night-sweats of phthisis. The oral administration of tellurium salts is followed by the deposition of the metal in all parts of the body. All living cells effect the reduction of tellurium salts to an ultra-microscopic form of the metal, which is slowly but continuously converted into methyl telluride  $[(\text{CH}_3)_2\text{Te}]$ . This alliaceous smelling substance is excreted in the breath, perspiration, urine and feces. When taken by mouth, the larger part of a tellurium salt is reduced to the metal which is excreted in the feces.

#### COMPOUNDS OF SELENIUM AND TELLURIUM

In many respects the compounds of selenium and tellurium remind one of the sulfur compounds. We will consider only the hydrides, oxides and oxygen acids.

**Hydrides.**—Hydrogen selenide ( $\text{H}_2\text{Se}$ ) is formed by the direct union of its constituent elements (1) or, better, by the action of dilute hydrochloric or sulfuric acids upon the selenides of the metal (2).



Hydrogen selenide is a colorless gas having a very offensive odor similar to that of decaying onions. It is less stable toward heat than hydrogen sulfide and its aqueous solution is a very weak acid. It precipitates selenides in the same manner as hydrogen sulfide precipitates sulfides.

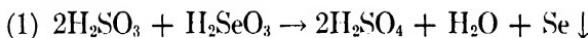
Hydrogen telluride is prepared in the same manner as hydrogen selenide. It is the least stable of the three hydrides of the sulfur

family. Its odor is likewise offensive. It is slightly soluble in water and precipitates tellurides of the heavy metals. Both of the hydrides are very poisonous. Because of the fact that these elements tend to accumulate in the systems of those working with them, they should be handled with care as they will undermine the health and cause foul-smelling breath.

**Oxides.**—When the metal is burned in air or in the presence of nitrogen dioxide and oxygen, selenium forms the dioxide ( $\text{SeO}_2$ ). Three other oxides are known, having the formulas  $\text{Se}_2\text{O}_3$ ,  $\text{Se}_3\text{O}_4$ , and  $\text{SeO}_3$ . The oxides are acidic in nature.

Tellurium dioxide ( $\text{TeO}_2$ ) is prepared in the same way as selenium dioxide. The trioxide ( $\text{TeO}_3$ ) is obtained as an orange-yellow powder by heating telluric acid,  $\text{H}_2\text{TeO}_4 \cdot 2\text{H}_2\text{O}$ .

**Oxygen Acids.**—Selenous acid,  $\text{H}_2\text{SeO}_3$ , is an unstable white solid, formed by heating the dioxide with water. It forms both selenites and hydrogen selenites, such as  $\text{Na}_2\text{SeO}_3$  and  $\text{NaHSO}_3$ . This acid is reduced by sulfurous acid (1).



Tellurous acid is obtained as a white powder when a solution of the element in nitric acid is poured into cold water. It is similar to selenous acid but, unlike the latter, is somewhat basic. Its properties are illustrated by its forming the following compounds: tellurium sulfate [ $\text{Te}(\text{SO}_4)_2$ ] and telluryl sulfate ( $\text{TeOSO}_4$ ).

Selenic acid ( $\text{H}_2\text{SeO}_4$ ) is formed by treating selenous acid with active oxidizing agents, such as potassium permanganate and chlorine (2), or by the oxidation of selenous acid with  $\text{HClO}_3$ .



Selenic acid acts very much like sulfuric acid. It has the distinction of being the only single acid which dissolves gold. It may be concentrated to a solution containing 95 per cent of  $\text{H}_2\text{SeO}_4$ . This solution decomposes at  $265^\circ\text{C}$ .

Telluric acid is formed by oxidizing tellurous acid with a mixture of nitric acid and chromic acid. When the resulting solution is evaporated, crystals of the formula  $\text{H}_2\text{TeO}_4 \cdot 2\text{H}_2\text{O}$  separate. When these crystals are heated above  $160^\circ\text{C}$ ,  $\text{H}_2\text{TeO}_4$  is produced. This acid is a good oxidizing agent.

## CHAPTER XLI

### CHROMIUM AND CHROMIUM COMPOUNDS

#### CHROMIUM

Symbol, Cr. Valence, II, III, VI. Atomic Weight, 52.01;  
Atomic Number, 24

**History and Occurrence.**—In 1762, Lehman discovered a red mineral in Siberia which he named crocoite. About 1797, Vauquelin and Klaproth, working independently, found this mineral to be a compound of lead in combination with an acid which they found to be an oxide of a new element. The name *chromium* (Greek, *χρῶμα*, color) was assigned to the latter because all of its compounds were found to be highly colored.

Chromium always occurs in combination in Nature. Its principal ore is *chromite* or *chrome iron ore* ( $\text{FeO} \cdot \text{Cr}_2\text{O}_3$ ), of which the largest deposits are found in southern Rhodesia, Turkey, New Caledonia, India, and Greece.<sup>1</sup> Chromite is widely distributed in and around serpentine and other basic rock areas in the United States. Such rocks are found in Pennsylvania, Maryland, North Carolina, western and central California, etc. Native lead chromate, *crocoite* ( $\text{PbCrO}_4$ ) is found chiefly in Siberia.

**Physical Properties.**—Chromium is a very hard, crystalline, silvery gray metal having a specific gravity of 6.92 at 20° C. It melts at about 161.5° C. and boils at 2200° C. It is non-magnetic and its ductility and malleability are very low.

**Chemical Properties.**—The chemical properties of chromium will be considered as (1) metallic chromium, (2) divalent chromium, (3) trivalent chromium, and (4) hexavalent chromium.

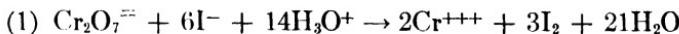
1. Metallic chromium does not oxidize (tarnish) in air, but when heated, it burns with a bright light in oxygen or in the oxyhydrogen flame and gives the sesquioxide ( $\text{Cr}_2\text{O}_3$ ). Chromium metal exists in an *active* and a *passive* form. The former is easily soluble in dilute acids with the evolution of hydrogen and the formation of blue chromous salts which are rapidly changed by the oxygen of the air to green chromic salts. However, if the metal is allowed to stand exposed to air, or is treated with chromic acid or concentrated nitric acid, it is changed to the *passive* form and as such is not acted upon by dilute acids.

2. Chromous ion is a divalent ion ( $\text{Cr}^{++}$ ) possessing a blue color. It is quite unstable, being readily converted to the chromic form. It is, therefore, a strong reducing agent. There are relatively few stable compounds containing the divalent form of chromium, the principal ones being the halogen salts (see Non-official Compounds,

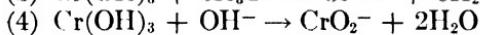
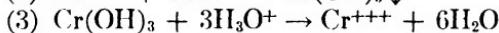
<sup>1</sup> Emmons: Principles of Economic Geology.  
( 576 )

p. 581) and the acetate. This form of chromium is rarely encountered and is of little importance.

3. Chromium exists more commonly in the trivalent form. The chromic salts are usually obtained by reducing dichromates in acid solution (1).



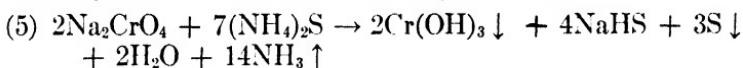
When chromic salts are treated with alkali hydroxides they yield chromic hydroxide (2). This hydroxide when treated with acids yields chromic salts (3) and when treated with alkali yields chromites (4).



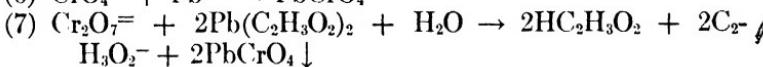
4. Hexavalent chromium is the form in which it occurs in most salts, and as such it exhibits an entirely non-metallic character. In the hexavalent form it exists with few exceptions either as chromate or dichromate.

Some of the characteristic reactions of chromates and dichromates are as follows:

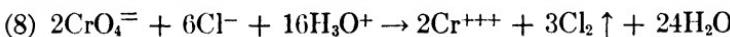
(a) *Chromates.*—1. When a neutral or alkaline solution of a chromate is treated with hydrogen sulfide or ammonium sulfide, chromium hydroxide and sulfur are precipitated (5).



2. Lead ion precipitates soluble chromates (6) or dichromates (7), free from mineral acids, as yellow lead chromate. The precipitate is soluble in hydrochloric acid and in fixed alkalies.

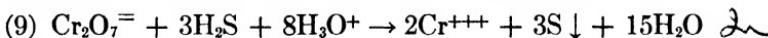


3. When a solution of a chromate is boiled with hydrochloric acid, the chromate is reduced to the chloride and chlorine is evolved (8).

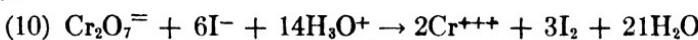


4. In the presence of NaOH, Cr(OH)<sub>3</sub> or CrO<sub>2</sub><sup>-</sup> are readily oxidized by H<sub>2</sub>O<sub>2</sub> or the halogens to CrO<sub>4</sub><sup>=2-</sup> which may be identified as yellow PbCrO<sub>4</sub> or as red Ag<sub>2</sub>CrO<sub>4</sub>.

(b) *Dichromates.*—1. Hydrogen sulfide reduces a dichromate in acid solution to a chromic salt and sulfur is precipitated (9).



2. When an acidulated solution of a dichromate is treated with hydrobromic or hydriodic acids, the respective halogen is set free (10).



**Official Tests for Identity.**—The official compendia do not find it necessary to give identification tests for any form of chromium except *Chromate* and *Dichromate*. Both of these when free of mineral acids respond to the same tests.

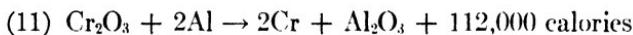
1. *Chromate* and *Dichromate* respond to the following tests:

(a) They yield with lead acetate T.S. a yellow precipitate of lead chromate (6) (7), which is insoluble in acetic acid.

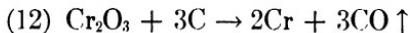
(b) When acidified with diluted sulfuric acid and treated with solution of hydrogen peroxide, a transient blue color is produced. Upon shaking the solution immediately with ether, the blue color passes into the ether layer. (For further discussion see Hydrogen Peroxide, p. 57.)

**Commercial Manufacture.**—1. When the mineral, chromite, is fused with sodium carbonate, sodium chromate ( $\text{Na}_2\text{CrO}_4$ ) is produced. This is leached out, converted to the dichromate, and electrolyzed to produce the metal.

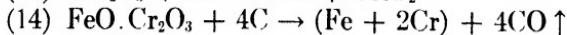
2. The commercial production of aluminum made it practical to use this metal in the reduction of the oxides of those metals that are not only difficult to reduce with carbon but also have a tendency to form carbides with the same. The application of *aluminothermy* (Goldschmidt method, *q. v.*) to the reduction of chromium oxide has made it possible to obtain a very high grade of chromium metal (11).



3. A method first employed by Moissan in 1894, yields an impure product which is unfit for use in hardening steel. The oxide ( $\text{Cr}_2\text{O}_3$ ) is reduced with carbon in an electric furnace (12) and the crude metal is freed from most of its carbide by heating with oxide.



4. When chrome iron ore or chromium oxide is reduced with carbon or silicon (13) in an electric furnace, an alloy of iron and chromium, known as *ferrochrome*, is produced (14).



**Pharmacological Action of Chromium Ion.**—The pharmacodynamic actions of chromium salts, chromates, and dichromates are very similar. They are destructive to tissue, regardless of whether applied topically or administered orally. When taken internally, they produce a characteristic nephritis and glycosuria. Persons exposed to "chromate dust" develop deep ulcers of the skin and the nasal mucosa that heal very slowly.

Chromium trioxide ( $\text{CrO}_3$ ) is a powerful oxidizing agent. It is used as a caustic. One to 3 per cent solutions are used as local astringents, whereas 0.2 to 0.5 per cent solutions are employed for urethral injections. The dichromates, especially potassium dichromate, have been used in the treatment of cancer.

**Uses.**—Chromium *as such* is never used in medicine. Chromium trioxide ( $\text{CrO}_3$ ) is sometimes employed as a caustic; in 2 to 3 per cent solution as an astringent; in 5 per cent solution for perspiring feet; and in 0.05 to 0.025 per cent solution for urethral injections. Potassium dichromate has been used ( $\frac{1}{10}$  to  $\frac{1}{8}$  grain) internally against gastric ulcer.

One of the principal industrial uses of chromium is in hardening steel, less than 1 per cent having a very material influence. High-speed cutting tools that will not lose their temper even at red heat contain both chromium and tungsten. The recently developed *stainless steels* contain as much as 13 per cent of chromium. Various alloys of chromium, *e. g.*, nickelchrome alloy (*nichrome*, *chromel*, etc.) are used for electrical resistances and for heat and acid-resisting apparatus.

**Chromium Plating.**—Metals are protected against corrosion in either one of two ways: First, they may be coated or “plated” with a thin, dense coating of some other more resistant metal or metals, *e. g.*, copper, nickel, chromium, which mechanically prevent the moisture of the air from penetrating to the base metal. Second, they may be protected electrochemically with metals such as zinc and cadmium. Because of their higher position in the electromotive series than iron, which is usually the base metal, they will consequently be the first to corrode.

Because the usual deposit of chromium is so porous, it does not afford much mechanical protection and, therefore, an intermediate coating of copper followed by nickel is employed. The chief advantages of chromium as a plating metal are that it is extremely hard, has a pleasing appearance, and does not oxidize at ordinary temperatures, thus remaining free from tarnish.

#### OFFICIAL CHROMIUM COMPOUNDS

##### CHROMIUM TRIOXIDE

*Chromium Trioxide*, U. S. P. XIII

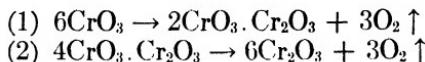
Formula,  $\text{CrO}_3$ . Molecular Weight, 100.01

**Physical Properties.**—Chromium trioxide occurs in long, needle-shaped crystals, in rhombic prisms having a metallic luster or in flakes. The color of the crystals ranges from a scarlet to a dark purplish-red. It is deliquescent in moist air. This oxide is a vigorous oxidizing agent, destroying both animal and vegetable tissues and, therefore, should not be brought in intimate contact with organic substances (sugar, charcoal, powdered vegetable drugs, etc.) as an explosion may occur.

One Gm. of chromium trioxide dissolves in 0.6 cc. of water at  $25^\circ \text{ C}.$ , giving a solution that apparently contains *dichromic acid*, a substance unknown in the pure state. One Gm. is soluble in 0.5 cc. of boiling water. When the hot saturated solution is cooled,

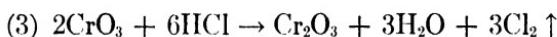
rose-red crystals of *chromic acid* ( $H_2CrO_4$ ) separate out. Chromium trioxide oxidizes organic solvents, *e. g.*, alcohol to acetaldehyde, so rapidly that the reaction may become dangerously violent. When warmed with hydrochloric acid, chlorine is evolved.

**Chemical Properties**—Chromium trioxide darkens when heated and at about  $196^\circ C.$  fuses to a reddish-brown liquid. At  $250^\circ C.$ , it loses oxygen and is converted into chromic chromate ( $CrO_3 \cdot Cr_2O_3$ ) (1). At higher temperatures it loses more oxygen, until a residue of green chromic oxide ( $Cr_2O_3$ ) remains (2).

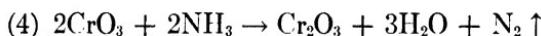


Chromic anhydride ( $CrO_3$ ) is analogous to sulfuric anhydride ( $SO_3$ ) and forms one series of salts (chromates,  $M_2CrO_4$ ) analogous to sulfates, and another series (dichromates,  $M_2Cr_2O_7$ ) which corresponds to the pyrosulfates.

When chromium trioxide is warmed with hydrochloric acid, chlorine is evolved (3).



Aminonia gas reduces chromium trioxide to chromic oxide ( $Cr_2O_3$ ), nitrogen and water (4).



**Official Tests for Identity.**—1. Chromium trioxide yields chlorine when warmed with hydrochloric acid (3).

2. Chromium trioxide responds to the tests for *Chromate* ion (*q. v.*).

**Commercial Manufacture.**—Chromium trioxide is prepared by adding concentrated sulfuric acid to a cold saturated solution of potassium chromate (5). The long needle-shaped red crystals are separated from the mother liquor and washed with concentrated nitric acid. The excess nitric acid is removed by means of a current of dry air.



**Pharmaceutical Preparations and Uses.**—1. *Chromium Trioxide* (Chromii Trioxidum, Chromic Anhydride, "Chromic Acid"), U. S. P. XIII.—"Chromium Trioxide contains not less than 98 per cent of  $CrO_3$ ." The U. S. P. cautions: *Chromium Trioxide should not be brought into intimate contact with organic substances, as serious explosions are likely to result.* The use has been discussed under Pharmacological Action of Chromium Ions, p. 578.

#### NON-OFFICIAL CHROMIUM COMPOUNDS

Chromium forms three principal series of compounds, *viz.*, chromous salts, corresponding to  $CrO$  (chromous oxide); chromic salts,

corresponding to  $\text{Cr}_2\text{O}_3$  (chromic oxide), and chromates, corresponding to  $\text{CrO}_3$  (chromium trioxide or chromic anhydride).

**Halogen Compounds.**—**Chromous Chloride** ( $\text{CrCl}_2$ ).—Chromous chloride occurs in white silky needles. It is made by reducing warm chromic chloride with hydrogen. It is readily soluble in water, giving a deep blue solution, which rapidly absorbs oxygen to form green chromic chloride ( $\text{CrCl}_3$ ). Nearly all chromous compounds are unstable and act as powerful reducing agents. The corresponding chromous iodide ( $\text{CrI}_2$ ) and bromide ( $\text{CrBr}_2$ ) have been made by heating the metal in hydrogen iodide or hydrogen bromide.

**Chromic Chloride** ( $\text{CrCl}_3$ ).—Chromic chloride is made by reducing the sesquioxide ( $\text{Cr}_2\text{O}_3$ ) with carbon in the presence of dry chlorine (1).

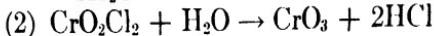
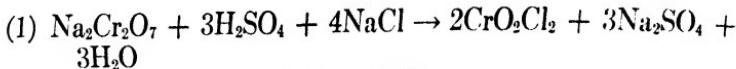


It forms anhydrous reddish-violet, lustrous scales (specific gravity, 2.76 at 20° C.) that are almost insoluble in water. The scales are easily soluble in water containing a trace of a reducing agent, *e. g.*,  $\text{CrCl}_2$ ,  $\text{SnCl}_2$ , etc., and produce *green* solutions from which *blue* crystals of the hexahydrate ( $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ ) deposit on standing. The blue crystals of the hexahydrate dissolve in water to give a *violet-colored* solution, which changes to *deep green* on boiling. The work of A. Werner and others indicates that the difference in the color of solutions of the hexahydrate is due to the relative positions of the chlorine and combined water in the molecule. It is thought that the blue variety dissociates into  $\text{Cr}(\text{H}_2\text{O})_6^{+++}$  and  $3\text{Cl}^-$ . This view is supported by the fact that silver nitrate acts normally with respect to the salt, *e. g.*, precipitates *all* of the chloride ions as silver chloride. From pale green solutions of the hexahydrate, silver nitrate precipitates only *two-thirds* of the chlorine, a fact which would indicate that this form dissociates into  $\text{CrCl}(\text{H}_2\text{O})_5^{++}$  and  $2\text{Cl}^-$ . Likewise, silver nitrate precipitates only *one-third* of the chlorine from solutions of the darker green variety, indicating dissociation into  $\text{CrCl}_2(\text{H}_2\text{O})_4^+$  and  $\text{Cl}^-$ . These reactions with silver nitrate suggest the following formulas for the respective hexahydrates: blue hexahydrate  $[\text{Cr}(\text{H}_2\text{O})_6\text{Cl}_3]$ , pale green form  $[\text{CrCl}(\text{H}_2\text{O})_5\text{Cl}_2 \cdot \text{H}_2\text{O}]$  and darker green variety  $[\text{CrCl}_2(\text{H}_2\text{O})_4\text{Cl} \cdot 2\text{H}_2\text{O}]$ .

**Chromic Bromide** ( $\text{CrBr}_3$ ).—Chromic bromide is prepared in the anhydrous form in much the same manner as the anhydrous chloride. Its properties closely resemble those of the latter.

**Oxyhalogen Chromium Compounds.**—Attention has been called to the tendency on the part of the members of this group to unite with oxygen and in such combination to act as metals to form salts, *e. g.*,  $\text{CrO}_2\text{Cl}_2$ ,  $\text{MoO}_2\text{F}_2$ ,  $\text{UO}_2(\text{NO}_3)_2$ , etc. Chromium forms such oxysalts with chlorine and fluorine, but the corresponding iodide and bromide are unknown. The former are apparently halogen derivatives of chromic anhydride. The *oxychloride* or *chromyl chloride* (boiling-point, 117° C., melting-point, 96.5° C.) is obtained as a heavy (density, 1.836), blood-red liquid by distilling a dichro-

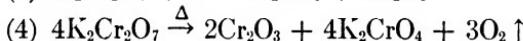
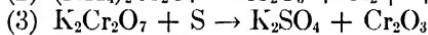
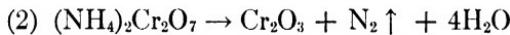
mate with sulfuric acid and sodium chloride (1). It is hydrolyzed by water to chromium trioxide and hydrochloric acid (2).



**Oxides and Hydroxides.**—**Chromous Oxide** ( $\text{CrO}$ ).—Chromous oxide is unknown in the anhydrous condition, but its monohydrate  $\text{CrO}\cdot\text{H}_2\text{O}$  or  $\text{Cr(OH)}_2$  may be prepared by adding a solution of potassium hydroxide in air-free water to a solution of chromous chloride. It is a brown, amorphous solid which rapidly oxidizes in air and, when heated, is decomposed into hydrogen and chromic oxide (1).

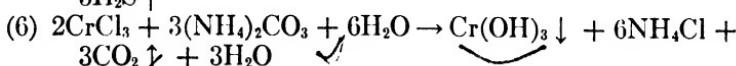
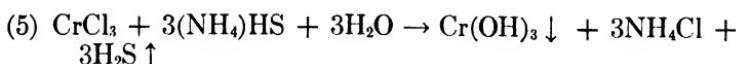


**Chromic Oxide or Sesquioxide** ( $\text{Cr}_2\text{O}_3$ ).—The native form of this oxide is known as *chrome ocher*. It may be obtained as a green, crystalline powder by (a) burning the metal in oxygen, (b) by igniting the corresponding hydroxide ( $\text{Cr}[\text{OH}]_3$ ), (c) by heating dry ammonium dichromate (2), or (d) by heating potassium dichromate either with (3) or without sulfur (4) and washing out the potassium sulfate (3).



After ignition, the oxide is almost insoluble in water, in acids and in dilute alkalies. When fused with silicates, it imparts a green color to them, hence its use in making "green" glass and china. The anhydrous oxide and its several hydrates are used as paint pigments (chrome green, emerald green, etc.).

**Chromic Hydroxide** [ $\text{Cr}(\text{OH})_3$ ].—Hydroxides precipitate gelatinous, blue chromic hydroxide from solutions of chromic salts. The blue color of the precipitate varies from a blue-green color when hot solutions and alkali hydroxides are used, to a pale blue color, when precipitation is effected in cold solutions with ammonium hydroxide. It is thought that the formula  $\text{Cr}_2\text{O}(\text{OH})_4$  or  $\text{Cr}_2\text{O}_3\cdot 2\text{H}_2\text{O}$  expresses the composition of the blue-green precipitate, and  $\text{Cr}(\text{OH})_3\cdot 2\text{H}_2\text{O}$  is the formula for the pale blue form. Ammonium hydrosulfide (5) and normal ammonium carbonate (6) precipitate chromium ( $\text{Cr}^{+++}$ ) as the hydroxide from solutions of chromic salts.



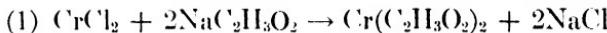
Chromic hydroxide is soluble in acids (7) and in alkali hydroxides (8).



**Chromium Salts.**—**Chromous Sulfate** ( $\text{CrSO}_4 \cdot 7\text{H}_2\text{O}$ ).—This rather unstable salt is isomorphous with ferrous sulfate, magnesium sulfate, etc. It is made by dissolving chromous acetate (*q. v.*) in dilute sulfuric acid with the aid of heat. On cooling, bluish crystals of chromous sulfate separate out. It is prepared also by dissolving metallic chromium in diluted sulfuric acid.

**Chromic Sulfate** [ $\text{Cr}_2(\text{SO}_4)_3 \cdot 15\text{H}_2\text{O}$ ].—Chromic sulfate is obtained in violet or green colored scales when chromic hydroxide is dissolved in dilute sulfuric acid and the resulting solution carefully concentrated to crystallization. The salt is soluble in water, but nearly insoluble in alcohol. It is usually shipped in wooden barrels and is used in the textile industries and for making green varnishes, inks, etc.

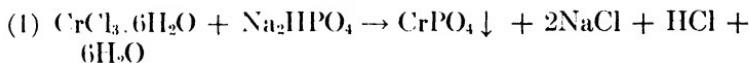
**Chromous Acetate** [ $\text{Cr}(\text{C}_2\text{H}_3\text{O}_2)_2 \cdot \text{H}_2\text{O}$ ].—Chromous acetate is prepared by pouring a solution of chromous chloride into a saturated solution of sodium acetate (1). This salt is the most stable chromous salt and therefore is used in making other chromous compounds. As a brownish-violet pasty mass, it is very easily oxidized and hence is used in gas analysis as an oxygen absorbent.



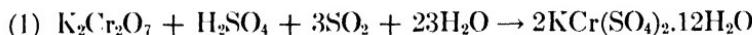
Chromic acetate [ $\text{Cr}(\text{C}_2\text{H}_3\text{O}_2)_3 \cdot \text{H}_2\text{O}$ ] is a greenish-gray powder, soluble in water. It is used as a mordant and in chrome tanning.

**Chromic Nitrate** [ $\text{Cr}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ ].—Chromic nitrate occurs in the form of purplish-red crystals. It is made by dissolving chromic hydroxide in nitric acid.

**Chromic Phosphate** ( $\text{CrPO}_4 \cdot 3\text{H}_2\text{O}$ ) (Plessy's or Arnaudon's Green).—Chromic phosphate is made by adding a solution of chromic chloride to a solution of sodium phosphate (1). It is a bluish-green powder and is used as a paint pigment.



**Chromic Alum or Chromium and Potassium Sulfate** [ $\text{KCr}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ ].—Chromic alum occurs in the form of dark, violet-red octahedral crystals. (See Alums.) It is made by reducing potassium dichromate in dilute sulfuric acid with sulfur dioxide (1).



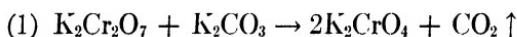
Chrome alum is used in the textile, dyeing, and tanning industries.

**Chromates.**—It has already been pointed out (p. 579) that when chromium trioxide ( $\text{CrO}_3$ ) is dissolved in hot water and the solution cooled, small rose-red crystals of *chromic acid* ( $\text{H}_2\text{CrO}_4$ ) separate out. This acid forms salts (chromates) that are analogous to those

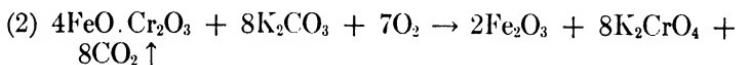
of sulfuric acid. Unlike sulfuric acid, however, chromic acid does not form acid or hydrogen salts, *e. g.*,  $\text{NaHCrO}_4$ . A possible explanation of this behavior is that *dichromates*, *e. g.*,  $(\text{Na}_2\text{Cr}_2\text{O}_7)$  are always formed in acid solutions of *chromates*. When an excess of a chromium compound is fused with a fixed alkali, *trichromates* ( $\text{Na}_2\text{Cr}_2\text{O}_7 + \text{CrO}_3 \rightarrow \text{Na}_2\text{Cr}_3\text{O}_{10}$ ) and even *tetrachromates* ( $\text{Na}_2\text{Cr}_2\text{O}_7 + 2\text{CrO}_3 \rightarrow \text{Na}_2\text{Cr}_4\text{O}_{13}$ ) are formed.

Chromic acid forms a number of both soluble and insoluble salts. The most important soluble chromates are those of potassium and sodium.

**Potassium Chromate** ( $\text{K}_2\text{CrO}_4$ ).—Potassium chromate occurs as stable, yellow, rhombic crystals. Its aqueous solutions are slightly alkaline to litmus. It is made by adding a weak alkaline solution of potassium carbonate to a hot aqueous solution of potassium dichromate until the mixture is slightly alkaline (1). The solubility of potassium chromate (1 part in less than 2 parts of water) necessitates the concentration of the liquid to a small volume before crystallization of the salt will begin.



Potassium chromate is made in large quantities from chrome iron ore. The finely ground ore is mixed with potassium carbonate and either calcium hydroxide or carbonate, and roasted in a reverberatory furnace (2). All of the iron is converted into oxide and potassium chromate is formed. The lime or chalk is added to prevent fusion of the mixture. When the oxidation is complete, the mass is lixiviated with water and the solution filtered, acidified with acetic acid, and concentrated.



It is used as an indicator in volumetric determinations of some silver compounds; as a mordant in dyeing; in the leather industry; and to harden and preserve anatomical specimens.

**Sodium Chromate** ( $\text{Na}_2\text{CrO}_4$ ).—Sodium chromate is a yellow, crystalline salt obtained in much the same manner as the potassium salt. It crystallizes with 10 molecules of water (mol. wt. 234.07) which are expelled above  $68^\circ \text{C}$ .  $\text{Na}_2\text{CrO}_4 \cdot 6\text{H}_2\text{O}$  is the stable form below  $19^\circ \text{C}$ . On account of its cheapness and greater solubility, sodium chromate has largely replaced potassium dichromate for industrial use.

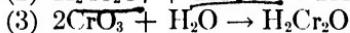
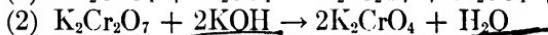
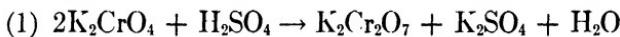
Lead, zinc, silver and barium form chromates that are only slightly soluble in water. They are colored compounds that are usually made by double decomposition. They are used largely as paint pigments.

**Lead Chromate** ( $\text{PbCrO}_4$ ).—Lead chromate occurs as a yellow powder which is known as *Leipzig-*, *King's-*, *Paris-*, *Cologne-* or *Chrome-yellow*. It is nearly insoluble in water but dissolves in

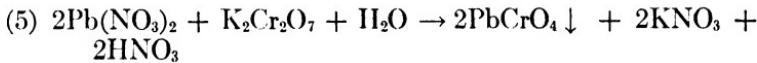
strong acids or bases. Several basic lead chromates are of industrial importance. For example, when chrome-yellow is boiled with a weak solution of potassium hydroxide, or when a fusion of potassium and sodium nitrates is added in small amounts at a time to yellow lead chromate, *chrome-red* ( $\text{PbO} \cdot \text{PbCrO}_4$ ) is formed. *Chrome-orange* is a mixture of chrome-red and chrome-yellow.

**Zinc Chromate** ( $\text{ZnCrO}_4$ ).—Zinc chromate is a yellow salt which is especially valuable as a paint pigment because of its being unaffected by hydrogen sulfide.

**Dichromates.**—It will have been noted that when chromate solutions are made acid their yellow color changes to the characteristic orange color of dichromates (1). Furthermore, when solutions of dichromates are made alkaline, their orange "dichromate" color changes to yellow (2). The dichromates are the salts of dichromic acid, which apparently is present in concentrated solutions of chromic anhydride (3). The dichromates are very powerful oxidizing agents, *e. g.*, 1 molecule of potassium dichromate when treated with an acid yields 3 atoms of active oxygen (4).



When a solution of a *dichromate* is added to a solution containing an ion which forms an insoluble *chromate*, a precipitate consisting of an insoluble *chromate* and *not a dichromate* is produced (5).



The most important dichromates are those of potassium and sodium.

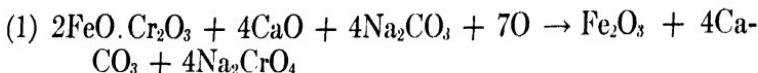
**Potassium Dichromate** ( $\text{K}_2\text{Cr}_2\text{O}_7$ ).—Potassium dichromate may be made by a process analogous to that used for preparing sodium dichromate (*q. v.*). It is made also by concentrating mixed solutions of sodium dichromate and potassium chloride. After the deposited sodium chloride has been filtered off, potassium dichromate crystallizes upon lead rods.

Potassium dichromate occurs in large, anhydrous, orange-red crystals. It is odorless, has a bitter metallic taste and is permanent in air. It is soluble in water (1 to 10) giving a distinctly acid solution. It is soluble in alcohol. It has a density of about 2.69 and melts at  $398^\circ \text{C}$ . At about  $500^\circ \text{C}$ ., it decomposes into potassium chromate, chromic oxide, and oxygen (1).



It is used in tanning (chrome-tanning), bleaching, dyeing, etc. It is a valuable oxidizing agent. In the light, it forms insoluble compounds with gelatin and gums, hence its use in photography as a "hardener" for gelatin films.

**Sodium Dichromate** ( $\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$ ).—Sodium dichromate is made by roasting powdered chrome iron ore in a reverberatory furnace with sodium carbonate and lime (1). The product consists of a mixture of iron oxide, calcium carbonate, and sodium chromate. The cooled material is lixiviated with a very dilute solution of sodium carbonate, the liquid filtered and, after being slightly acidified with sulfuric acid, concentrated to crystallization.



Sodium dichromate is a deliquescent, crystalline solid having a density of 2.52. At  $100^\circ \text{ C.}$ , it loses 2 molecules of water and then melts at  $320^\circ \text{ C.}$  At higher temperatures it decomposes (see Potassium Dichromate).

Because of its lesser cost and greater solubility, sodium dichromate has replaced potassium dichromate to a large degree for industrial purposes.

**Perchromic Acids.**—Several perchromic acids, *viz.*, (1)  $\text{H}_7\text{CrO}_{10}$ , (2)  $\text{H}_3\text{CrO}_7$  and (3)  $\text{H}_3\text{CrO}_8$  have been described. These acids readily decompose and evolve oxygen. In acid solution ( $\text{H}_2\text{SO}_4$ ),  $\text{H}_7\text{CrO}_{10}$  decomposes into chromic sulfate [ $\text{Cr}_2(\text{SO}_4)_3$ ] and oxygen. Perchromic acid (blue) is formed when hydrogen dioxide is treated with a solution of a dichromate acidified with sulfuric acid. It is very soluble in ether and in acid solution.

## CHAPTER XLII

### MOLYBDENUM, TUNGSTEN AND URANIUM AND THEIR COMPOUNDS

#### MOLYBDENUM

Symbol, Mo. Valences, II to VI. Atomic Weight, 95.95;  
Atomic Number, 42

**History and Occurrence.**—For many years, graphite, molybdenum sulfide, and other substances similar in appearance to lead were designated by the Greek word *μόλυβδος* (lead). Cronstedt differentiated between graphite and molybdenum sulfide and, in 1778, Scheele obtained molybdic acid from the sulfide. The pure metal was first obtained by Hjelm in 1780.

The native sulfide, *molybdenite* ( $\text{MoS}_2$ ), is the principal ore of molybdenum. It occurs widely distributed in Nature but in rather small quantities. In the United States it is found in Maine, Utah, Arizona, etc. There is also an apparently inexhaustible source of molybdenum ores in the mountains of Colorado. Other minerals containing molybdenum are *wulfenite* ( $\text{PbMoO}_4$ ), *molybdite* ( $\text{MoO}_3$ ) and a hydrated ferric *molybdate ocher*. Molybdenum is present in many iron ores.

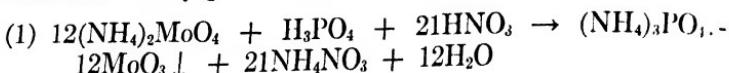
**Physical and Chemical Properties.**—Molybdenum is a malleable, silvery white metal. It is permanent in air. It crystallizes in the regular system, has a density of 10.2, melts at  $2620^\circ \text{ C}$ . and boils at  $3700^\circ \text{ C}$ . It is not as hard as glass but is harder than topaz.

When heated above  $600^\circ \text{ C}$ . in air, molybdenum is converted into the trioxide. It forms many compounds in which it exercises valences from 2 to 6. Like the other members of this family, it forms oxychlorides ( $\text{MoO}_2\text{Cl}_2$ ). The group tendency to form poly-salts containing a large excess of acidic anhydride  $[(\text{NH}_4)_3\text{PO}_4 \cdot 12\text{MoO}_3]$  is very pronounced in molybdenum. The metal is soluble in nitric or nitrohydrochloric acids. It forms a blue solution when dissolved in concentrated sulfuric acid. When this solution is heated it becomes colorless, evolves sulfur dioxide and precipitates molybdenum trioxide. The metal is insoluble in hydrochloric, hydrofluoric, and dilute sulfuric acids.

**Tests for Identity.**—1. When a dry molybdenum compound is heated on a platinum foil with concentrated sulfuric acid until nearly all of the acid is driven off, a blue residue remains.

2. Sodium phosphate precipitates yellow ammonium phosphomolybdate from warmed solutions of molybdates acidified with nitric acid (1). The precipitate is soluble in ammonia T.S. The composition of this precipitate varies with the conditions under which it is formed. When dried at  $130^\circ \text{ C}$ ., it has the formula

$(\text{NH}_4)_3\text{PO}_4 \cdot 12\text{MoO}_3$ . Arsenates, silicates, and tungstates interfere with this test as they give analogous precipitates.



3. When a solution of a molybdate is treated with zinc and sulfuric acid, a blue coloration is produced. The blue color of the solution gradually turns a greenish-gray and finally brown.

**Commercial Manufacture.**—Metallic molybdenum is made by first roasting the disulfide and leaching the resulting trioxide with ammonia water to form ammonium molybdate  $[(\text{NH}_4)_2\text{MoO}_4]$  which, in turn, is ignited to  $\text{MoO}_2$ . This is reduced to the metal with carbon in an electric furnace or by the Goldschmidt process (*q. v.*). When prepared in this manner, molybdenum metal is a gray powder which at a very high temperature (about  $2620^\circ \text{ C}.$ ) fuses into a silvery white mass.

**Uses.**—Molybdenum is never used in medicine. Its principal industrial use is in the manufacture of special grades of very tough and hard steel. It is also used in catalytic work. Because of the great demand for molybdenum metal in electronic tubes as a support wire for lamp filaments, lead-in wires, plates, grids, etc., during World War II, the production of molybdenum increased sixteen times over the period 1938 to 1944.

### MOLYBDENUM COMPOUNDS

Molybdenum unites with oxygen to form a number of oxides, the most important of which are  $\text{MoO}$ ,  $\text{Mo}_2\text{O}_3$ ,  $\text{MoO}_2$  and  $\text{MoO}_3$ . The first three of these oxides are prepared by processes that involve the reduction of molybdates or polymolybdates.

*Molybdenum trioxide* ( $\text{MoO}_3$ ) is by far the most interesting because it is the anhydride of molybdic acid ( $\text{H}_2\text{MoO}_4$ ) from which the various salts and polysalts of this element are obtained. This oxide is a white powder that turns yellow on heating and melts at  $795^\circ \text{ C}.$  Its density is 4.5. It is only slightly soluble in water, but dissolves readily in ammoniacal solution. When this ammoniacal solution is made acid with nitric acid, white, shining, hexagonal crystals of molybdic acid ( $\text{H}_2\text{MoO}_4$ ) separate out. Molybdic acid forms a number of salts known as molybdates, which have a marked tendency to pass into the polymolybdates. These polysalts contain a large excess of molybdic anhydride and have the property of combining with other oxides, *e. g.*, the oxides of phosphorus, arsenic, etc., to form very complex compounds.

Molybdenum forms di- ( $\text{MoCl}_2$ ), tri- ( $\text{MoCl}_3$ ), tetra- ( $\text{MoCl}_4$ ) and penta- ( $\text{MoCl}_5$ ) compounds with chlorine, bromine, and iodine. It forms halogen derivatives of molybdic anhydride, *e. g.* ( $\text{MoO}_2\text{F}_2$ ).

Molybdenum combined with sulfur ( $\text{MoS}_2$ ) is found in Nature in the mineral *molybdenite*. *Molybdenum disulfide* is a black, crystalline (hexagonal) powder, resembling graphite in appearance. Its

density is 4.8 and its melting-point 1185° C. It may be made by heating together molybdenum trioxide and sulfur. It is readily oxidized to the trioxide by roasting or by treating with nitric acid. When strongly heated in a current of hydrogen, it is reduced to metallic molybdenum. *Molybdenum trisulfide* ( $\text{MoS}_3$ ) is obtained as a brown powder by saturating a solution of an alkali molybdate with hydrogen sulfide and then adding a mineral acid. It is converted into the disulfide by heating in air.

**Uses.**—Molybdenum oxide (3 mg.) together with ferrous sulfate (195 mg.) in a specially co-precipitated complex in the form of tablets, are marketed as a hematinic preparation (Mol-Iron). The principal use, however, of molybdenum compounds is for the detection and quantitative determination of phosphates. When phosphates are added to a warm nitric acid solution of ammonium molybdate, they produce a yellow precipitate of complex ammonium phospho-molybdate (*q. v.*). This precipitate dissolves in alkalies and in an excess of phosphoric acid. It is insoluble in dilute mineral acids.

### TUNGSTEN (WOLFRAM)

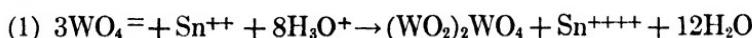
Symbol, W. Valence, II to VI. Atomic Weight, 183.92; Atomic Number, 74

**History.**--In 1781, Scheele and Bergman detected this element in scheelite, and in 1783, Juan José and d'Elhujar found it in wolfram.

**Occurrence.**—Tungsten is found in Nature as *wolframite*, a ferrous manganese tungstate ( $\text{FeWO}_4 \cdot \text{MnWO}_4$ ), as *wolfram ocher* or tungsten trioxide ( $\text{WO}_3$ ), as *scheelite* or calcium tungstate ( $\text{CaO} \cdot \text{WO}_3$ ) and as metallic tungstates, such as *lead tungstate* ( $\text{PbO} \cdot \text{WO}_3$ ), *barium tungstate* ( $\text{BaO} \cdot 4\text{WO}_3 \cdot 9\text{H}_2\text{O}$ ), *copper tungstate* ( $\text{CuO} \cdot \text{WO}_3$ ), etc.

**Properties.**—Tungsten is a very hard, brittle, silver-white to steel-gray, lustrous metal. It has a density of 19.3, melts at about 3370° C., which is the highest melting-point of any metal. It boils at 5900° C. By proper treatment, the metal becomes very ductile and then may be drawn into fine wires. The metal resists attack by most chemical agents. It is readily attacked by a mixture of hydrofluoric and nitric acids. By fusion with sodium carbonate or a mixture of sodium nitrate and sodium hydroxide it is converted into the soluble sodium tungstate ( $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$ ).

**Tests for Identity.**—Soluble tungstates or phosphotungstates are reduced by stannous chloride to the insoluble yellow tungsten trioxide. When this precipitate is heated with hydrochloric acid, it changes to a blue color (1).



Solutions of tungstates, when evaporated to dryness with hydrochloric acid, leave a yellow residue which is soluble in ammonia test solution.

**Metallurgy.**—Tungsten is obtained by fusing its ores with sodium carbonate and leaching out the sodium tungstate so produced with water. This solution is treated with an acid which precipitates tungstic acid ( $H_2WO_4 \cdot H_2O$ ). The tungstic acid is either ignited to the oxides which are subsequently reduced by hydrogen in an electric furnace or it is reduced to the metal by the Goldschmidt process (*q. v.*). The gray powder which results is compressed into bars and heated to a very high temperature in an electric furnace. These heated bars of metal are swaged and worked into slender rods which are sufficiently ductile to be drawn out into very fine wires.

**Uses.**—The high melting-point of this metal, together with its low volatility (less than carbon), makes it admirably suited for filaments in electric light bulbs. These tungsten filaments require only 1.25 watts per candle power, whereas the old carbon filaments needed 3.25 watts per candle power. Tungsten imparts great hardness to steel. These steels retain their temper even at red heat and are used in high-speed cutting tools. A new German product, called *widia metal*, is composed of tungsten carbide, cobalt, and carbon. In the United States it is called "Carballoy." It is said to be very much harder than any of the tungsten steels and to very nearly approach the hardness of diamond. The advent of this new alloy may revolutionize shop work in the same way that tungsten steels (Taylor-White steel) did nearly fifty years ago. Large quantities of tungsten are used in place of platinum for electrical contact points.

#### COMPOUNDS OF TUNGSTEN

The principal compound of tungsten is the trioxide ( $WO_3$ ). It is prepared either by decomposing hot solutions of tungstates with nitric acid or by igniting tungstic acid. It is insoluble in acids, but dissolves in alkalies to form a series of normal tungstates and also a series of polytungstates, which are the salts of simple tungstic acid and complex tungstic acid, respectively.

Tungstic acid, like the corresponding acids of molybdenum and uranium, forms complex compounds with phosphoric, arsenic, antimonie, boric, and vanadic acids. The U. S. Pharmacopoeia XIII recognizes *phosphotungstic acid* as a reagent. On account of the insolubility of its alkaloidal salts, this acid is used as a qualitative reagent for alkalioids. This complex acid occurs as white or yellowish-green crystals or as a crystalline powder. The approximate formula  $P_2O_5 \cdot 24WO_3 \cdot (H_2O)_n$  has been assigned to it. It dissolves in water and in alcohol but it is only slightly soluble in ether.

#### URANIUM

Symbol, U. Valence, IV, VI. Atomic Weight, 238.07;  
Atomic Number, 92

**History.**—In 1789, Klaproth obtained from pitchblende a yellow oxide which he considered to be the oxide of a new metal. He named

the element *uranium* after the planet, Uranus, which Herschel only recently had discovered. In 1823, Berzelius prepared some of the uranyl salts. He thought that the radical, uranyl ( $\text{UO}_2$ ), was the true metal. This misconception was disproven by Péligot in 1840.

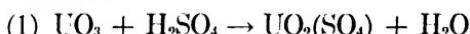
**Properties.**—Metallic uranium is a white metal resembling nickel in appearance. It has a density of 18.7 and a melting-point greater than  $1850^\circ \text{ C}$ . Uranium acts as a true metal by displacing the hydrogen of acids. The element and also its compounds are radioactive.

**Metallurgy.**—A large quantity of uranium is obtained from pitchblende by first roasting the ore to drive off any sulfur and arsenic and then converting the metals into sulfates by treating the purified ore with hot concentrated nitric acid followed by evaporation with sulfuric acid. The residue of mixed sulfates is lixiviated with water which dissolves out the soluble uranium and other sulfates but leaves the silica, insoluble lead sulfate, etc. After filtration, hydrogen sulfide is passed through the solution. This precipitates any arsenic, iron, copper, etc., present in the liquid. The filtrate is boiled with nitric acid and uranium, iron, and aluminum are precipitated by the addition of an excess of ammonium hydroxide. The well-washed precipitate is then digested with a warm concentrated solution of ammonium carbonate. This effects the solution of the uranium as ammonium uranate and leaves behind the hydrated oxides of iron, aluminum, etc., which are filtered off. When the liquid is concentrated and cooled, crystals of ammonium uranate separate out. These crystals yield a mixed oxide when ignited in a platinum crucible. These oxides are usually purified by dissolving them in nitric acid and then precipitating the uranium as the oxalate with oxalic acid. When uranyl oxalate ( $\text{UO}_2 \cdot \text{C}_2\text{O}_4$ ) is ignited, it yields a much purer mixture of oxides,  $\text{U}_3\text{O}_8$  or  $\text{UO}_2 \cdot 2\text{UO}_3$ . When the oxide is heated with coke in an electric furnace, a uranium metal of about 98 per cent purity is obtained.

A very pure metal may be obtained also by the reduction of uranous chloride ( $\text{UCl}_4$ ) with metallic sodium.

### COMPOUNDS OF URANIUM

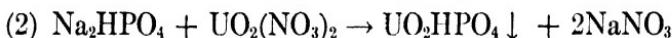
Uranium forms two principal oxides, *viz.*, uranous oxide or uranyl ( $\text{UO}_2$ ) and uranic oxide ( $\text{UO}_3$ ). The former is basic in character, whereas the latter is both acid- and base-forming (amphoteric). These two oxides are the sources of several series of salts. When the basic oxide is dissolved in acids, it forms normal *uranous* salts, *e. g.*,  $\text{UCl}_4$ ,  $\text{U}(\text{SO}_4)_2$ ,  $\text{UI}_4$ , etc. The uranous salts are quite unstable. They are active reducing agents. Uranic oxide ( $\text{UO}_3$ ) dissolves in acids to form the basic *uranyl* salts in which the  $\text{UO}_2$  radical acts as a metal (1).



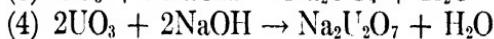
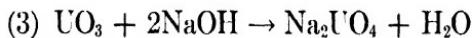
Uranyl nitrate ( $\text{UO}_2[\text{NO}_3]_2 \cdot 6\text{H}_2\text{O}$ ) was official as *Uranii Nitras* in the ninth revision of the U. S. Pharmacopœia. This efflorescent,

radioactive salt occurs in light yellow prisms which are odorless but have a bitter astringent taste. It is soluble in 1.2 parts of water at 25° C. and freely soluble in alcohol and in ether. Because of its slight radioactivity, this salt was given in 10-mg. ( $\frac{1}{6}$ -grain) doses in the treatment of spreading sluggish ulcers. It was directed to be used with caution.

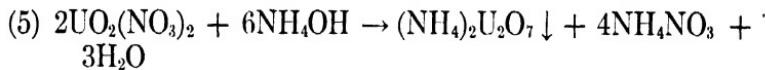
Uranyl nitrate is used in the volumetric determination of phosphoric acid (2). Glass, made by adding uranium nitrate or any other uranium salt to the melt, has a greenish-yellow fluorescence.



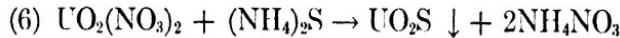
Uranic oxide dissolves in alkalies to form *uranates* (3) and *diuranates* (4), which correspond to the chromates and dichromates.



In the presence of ammonium chloride, ammonium hydroxide precipitates ammonium diuranate from a solution of a uranyl salt (5).



Ammonium sulfide precipitates an unstable, brown uranyl sulfide ( $\text{UO}_2\text{S}$ ) from solutions of a uranyl salt (6).



## CHAPTER XLIII

### MANGANESE AND MANGANESE COMPOUNDS

#### MANGANESE

Symbol, Mn. Valences, II, IV, VI, VII. Atomic Weight, 54.93; Atomic Number, 25

**History.**—Pyrolusite, a naturally occurring manganese dioxide, has been known from early times. This substance was thought to be a magnetic oxide of iron or magnetite until in 1740, J. H. Pott showed that this ore did not contain iron and that a definite series of salts could be obtained from it. In 1774, C. Scheele showed it to be an oxide of a new element and in the same year, J. G. Gahn isolated the metal.

**Occurrence.**—Manganese is chemically and geologically related to iron and hence is frequently found in Nature associated with it. Average igneous rocks contain about 0.078 per cent of manganese. *Pyrolusite*, native  $\text{MnO}_2$ , is the principal manganese ore. It occurs widely distributed. Manganese is the chief constituent of the following minerals: *Pyrochroite* ( $\text{MnO} \cdot \text{H}_2\text{O}$ ), *wad* (impure oxides), *manganite* ( $\text{Mn}_2\text{O}_3 \cdot \text{H}_2\text{O}$ ), *polianite* ( $\text{MnO}_2$ ), *hausmannite* ( $\text{Mn}_3\text{O}_4$ ) and *psilomelane* ( $\text{Mn}_2\text{O}_3 + \text{H}_2\text{O}$ ). Manganese occurs as the sulfate in *mallardite* ( $\text{MnSO}_4 \cdot 7\text{H}_2\text{O}$ ), as the sulfide in *alabandite* ( $\text{MnS}_3$ ), as the carbonate in *rhodochrosite* ( $\text{MnCO}_3$ ), and as the silicate in *rhodonite* ( $\text{MnSiO}_3$ ).

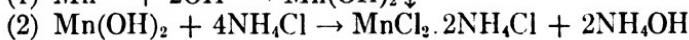
Traces of manganese occur in almost all organs of both man and animals. The smaller part of this manganese is derived from vegetable foods, whereas the larger amount comes from animal sources.

**Physical Properties.**—Manganese is a very hard, brittle, lustrous, gray-white metal resembling cast-iron in appearance. It has a density of about 7.2. It melts at about  $1260^\circ\text{C}$ . and boils at about  $1900^\circ\text{C}$ .

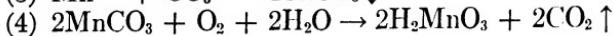
**Chemical Properties.**—The pure metal oxidizes readily in moist air, but its alloys containing iron resist oxidation. Manganese decomposes steam, whereas water at  $23^\circ\text{C}$ . is decomposed by the finely divided metal. It reacts with dilute acids and liberates hydrogen and forms manganous salts.

Solutions of the manganous salts exhibit the following reactions:

1. When a fixed alkali is added to a solution of the manganous salt, a white precipitate of manganous hydroxide is produced (1). The precipitate soon darkens by absorption of oxygen from the air and is converted into hydrated manganic hydroxide [ $\text{MnO(OH)} \cdot \text{Mn}_2\text{O}_3 \cdot \text{H}_2\text{O}$ ]. Manganous hydroxide is soluble in an excess of ammonium salts (2).



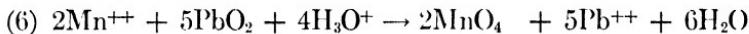
2. Alkali carbonates precipitate white manganous carbonate from solutions of manganous salts (3). The precipitate turns brown on exposure to air, due to the formation of hydrated manganic hydroxide (4).



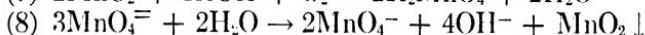
3. Ammonium sulfide precipitates salmon colored manganous sulfide from neutral solutions of manganous salts and turns freshly precipitated manganous hydroxide into sulfide (5). The precipitate is soluble in acetic and in diluted mineral acids.



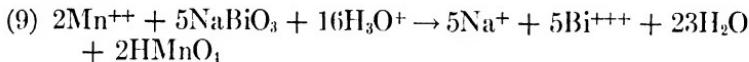
4. When a small quantity of a manganese compound (not the dioxide) is heated to boiling with diluted nitric acid and a little brown oxide of lead, the supernatant liquid will have a reddish-purple color, due to permanganic acid (6).



5. When a manganese compound is fused on a porcelain crucible cover with a little potassium chlorate and potassium hydroxide, the melt becomes dark green (7). When the mass is lixiviated with water and the solution acidified, the color changes to a reddish-purple (8).



6. Sodium bismuthate (approx.  $\text{NaBiO}_3$ ) in nitric acid solution will oxidize  $\text{Mn}^{++}$  to purple  $\text{MnO}_4^-$  ion (9). Provided nothing is present to react with the permanganate ion, this is a very delicate test for manganese.



7. Manganese compounds impart an amethyst color to a borax bead.

**Commercial Manufacture.**—The various oxides of manganese are difficult to reduce even at high temperatures with hydrogen. A very crude metal may be obtained by reducing the oxide with carbon in an electric furnace. Various processes have been recommended for the reduction of manganese oxides (Brunner, Glatzel, Moissan, etc.), but the one most generally used is the "thermite" method of H. Goldschmidt (*q. v.*).

Commercial alloys of manganese and iron are made by reducing the respective ores in a blast furnace. *Ferromanganese* (25 to 85 per cent of Mn) and *spiegeleisen* (12 to 33 per cent of Mn) are examples of manganese alloys.

**Pharmacological Action of Manganese Ions.**—When orally administered, manganese salts (not permanganates) produce no noticeable

effects. A small quantity of the manganese is absorbed from the alimentary tract and is deposited principally in the kidneys and liver. It is excreted as sulfide in the feces. It has never been shown that manganese exercises any hematinic action. It is sometimes prescribed with iron because of its possible synergistic action.

The permanganates are powerful oxidizing agents. Solutions containing from 0.02 to 0.1 per cent are used for urethral injections. Large doses of permanganates produce very severe gastro-enteritis.

**Uses.**—Manganese is used in the preparation of its salts. Manganese alloys containing less than 7 per cent of this metal are soft and ductile but, as the per cent of manganese increases, they become hard and brittle. Manganese steel, containing from 7 to 20 per cent of manganese, is very hard and hence is used in making burglar-proof safes, armor plate, and crushing and grinding machinery. Various alloys of manganese containing copper, zinc, nickel, etc., are of industrial importance.

Manganese compounds are used in the manufacture of glass, colored bricks, dryer in paints and varnishes, dry cells, chemicals, etc.

#### OFFICIAL MANGANESE COMPOUNDS

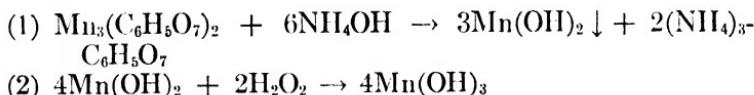
##### MANGANOUS CITRATE

*Soluble Manganese Citrate*, N. F. VIII

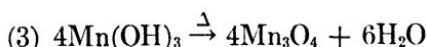
Formula,  $Mn_3(C_6H_5O_7)_2$ . Molecular Weight, 542.99

**Physical Properties.**—Soluble manganese citrate occurs as a pale orange or pinkish-white powder, as granules, or as translucent scales, and is permanent in the air. It is odorless, and has a slightly bitter, astringent taste. Normal manganese citrate is only slightly soluble in water. However, the official soluble manganese citrate includes sodium citrate and is soluble in about four times its weight of water at 25° C. It is almost insoluble in alcohol but is soluble in boiling water.

**Chemical Properties.**—The chemical properties of a solution of soluble manganese citrate are characteristic of the manganous ion (*q. v.*). Ammonium hydroxide readily precipitates manganous hydroxide (1) which is oxidized to manganic hydroxide with hydrogen peroxide (2). The assay is based upon these reactions.



Upon igniting the  $Mn(OH)_3$ , manganous-manganic oxide is formed (3).



Solutions of the salt respond to the reactions for citrate.

**Official Tests for Identity.**—1. Manganous salts in solution yield a salmon-colored precipitate with ammonium sulfide T.S. (4).



The MnS is soluble in acetic acid.

2. Tests for the citrate are discussed under sodium citrate (see p. 182).

**Commercial Manufacture.**—It is prepared by the interaction of manganous hydroxide and citric acid. The excess citric acid is neutralized with sodium carbonate and the solution evaporated.

**Pharmaceutical Preparations and Uses.**—1. *Soluble Manganese Citrate* (Mangani Citras Solubilis, Manganese and Sodium Citrate), N. F. VIII.—Soluble Manganese Citrate is manganous citrate rendered soluble by means of sodium citrate, and contains not less than 48 per cent and not more than 52 percent of  $[\text{C}_3\text{H}_4\cdot\text{OH}\cdot(\text{COO})_3]_2\text{Mn}_3$ .

Because a trace of manganese is essential to health, it has been used for many years as a tonic. The role of manganese in the animal body is unknown. There has been some evidence that manganese is beneficial in certain types of anemia but it is considered by most physicians to have little real value in the treatment of disease. Average dose—0.2 Gm. (approximately 3 grains).

2. *Peptonized Iron and Manganese Solution* (Liquor Ferri Peptonati et Mangani, Solution of Iron Peptone and Manganese), N. F. VIII.—Peptonized Iron and Manganese Solution yields, from each 100 cc., not less than 0.265 Gm. and not more than 0.325 Gm. of Fe. The action of manganese in increasing the hematitic effect of iron has been reported to be similar to that of arsenic<sup>1</sup> and copper (*q. v.*). Albumin or protein was also found to be beneficial, hence the use of peptonized iron. Regardless of some evidence in favor of manganese, it is prescribed by only a few physicians. Average dose—8 cc. (approximately 2 fluidrachms).

## MANGANESE GLYCEROPHOSPHATE

*Manganese Glycerophosphate*, N. F. VIII

Formula,  $\text{MnC}_3\text{H}_5(\text{OH})_2\text{PO}_4$ . Molecular Weight, 225

**Physical Properties.**—It is a white or pinkish powder, having no odor and almost no taste. In the presence of citric acid (1 in 4), normal manganese glycerophosphate is soluble in about five times its weight of water at 25° C. It is insoluble in alcohol and slightly soluble in water.

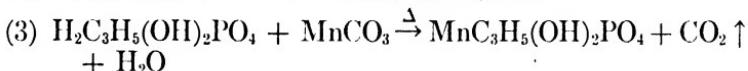
**Chemical Properties.**—A solution of manganese glycerophosphate in diluted hydrochloric acid has the characteristic properties of the manganese ion (*q. v.*) and glycerophosphate ion.

**Official Tests for Identity.**—1. Manganese glycerophosphate (1 in 20) in diluted hydrochloric acid responds to the reactions for manganese (see Manganese Citrate, p. 596), and for *Glycerophosphate* (see p. 186).

2. Potassium bisulfate dehydrates and decomposes the glycerophosphate portion of the compound when mixed with it and heated, producing pungent vapors of acrolein (1).



**Commercial Manufacture.**— Manganese glycerophosphate is obtained from manganese carbonate and glycerophosphoric acid (3). This acid is prepared by heating together glycerin and metaphosphoric acid (2).



**Pharmaceutical Preparations and Uses.**— 1. *Manganese Glycerophosphate* (Mangani Glycerophosphas), N. F. VIII.—Manganese Glycerophosphate, when dried to constant weight at 110°, contains not less than 98 per cent of  $\text{MnC}_3\text{H}_5(\text{OH})_2\text{PO}_4$ . The use of glycerophosphates is discussed under sodium (see p. 186). Because of the therapeutic reputation (doubtful) of manganese and glycerophosphate, these two appeared to be a logical tie-up for use as a tonic. The product is considered of little value, however, and finds practically no medical use except in proprietaries. Average dose—0.2 Gm. (approximately 3 grains).

2. *Compound Glycerophosphates Elixir* (Elixir Glycerophosphatum Compositum, Compound Glycerophosphates Solution), N. F. VIII.—This elixir contains 2 Gm. of Manganese Glycerophosphate per liter of elixir. (See also, p. 188.) Average dose—8 cc. (approximately 2 fluidrachms).

### MANGANESE HYPOPHOSPHITE

#### *Manganese Hypophosphite*, N. F. VIII

Formula,  $\text{Mn}(\text{H}_2\text{PO}_2)_2 \cdot \text{H}_2\text{O}$ . Molecular Weight, 202.94

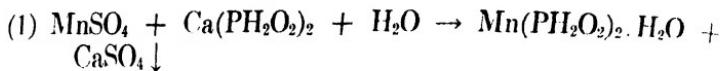
**Physical Properties.**— Manganous Hypophosphite is an odorless and nearly tasteless, granular or crystalline, pink powder. It is stable in air, dissolves in about 6.5 cc. of water at 25° C., or in about 6 cc. of boiling water. It is insoluble in alcohol.

**Chemical Properties.**— A water solution of manganous hypophosphite exhibits the chemical properties of the manganous ion (*q. v.*) and the hypophosphite ion.

**Official Tests for Identity.**— An aqueous solution of manganese hypophosphite (1 in 20) responds to the test with ammonium sulfide (*q. v.*) for manganous ion. The solution, heated, responds to the test with mercuric chloride T.S. and copper sulfate T.S. for hypophosphite ion (see p. 195).

**Commercial Manufacture.**— It is made by mixing a solution of calcium hypophosphite with a solution of manganous sulfate (1).

The mixture is allowed to stand in a warm place to permit the calcium sulfate to crystallize out, filtered, and either evaporated to crystallization or granulated.



**Pharmaceutical Preparations and Uses.**—1. *Manganese Hypophosphate* (Mangani Hypophosphis), N. F. VIII.—Manganese Hypophosphate, when dried for two hours over sulfuric acid, contains not less than 97 per cent of  $\text{Mn}(\text{H}_2\text{PO}_2)_2 \cdot \text{H}_2\text{O}$ . Caution should be observed in compounding this salt with oxidizing agents such as nitrates and chlorates, as explosions may occur if it is triturated or heated.

Hypophosphites, like the glycerophosphates, have enjoyed considerable unwarranted medicinal popularity. The compound is used for the supposed tonic benefits of manganese and hypophosphate (see p. 196).

2. *Compound Hypophosphites Syrup* (Syrupus Hypophosphitum Compositus), N. F. VIII.—The syrup contains 2.2 Gm. of manganese hypophosphate in 1 liter (see p. 197). Average dose—8 cc. (approximately 2 fluidrachms).

#### NON-OFFICIAL MANGANESE COMPOUNDS

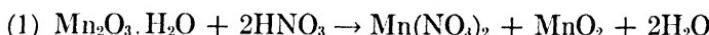
**Oxides and Hydroxides.**—**Manganous Oxide** ( $\text{MnO}$ ).—Manganous oxide is formed as a greenish-gray powder when manganous carbonate or oxalate is heated, or when one of the higher oxides of manganese is carefully reduced with hydrogen or carbon monoxide. It is decidedly basic and dissolves in acids to form the corresponding manganous salts. When heated, it is converted into dull red mangano-manganic oxide ( $\text{Mn}_3\text{O}_4$ ) which is native as hausmannite. It is used in the preparation of manganous compounds, in analytical chemistry, and in the textile industry.

**Manganous Hydroxide** [ $\text{Mn}(\text{OH})_2$ ].—Manganous hydroxide is formed as a white flocculent precipitate when an alkali hydroxide is added to a solution of a manganous salt. The precipitate is unstable and gradually absorbs oxygen from the air to form brown, hydrated manganic hydroxide [ $\text{Mn}(\text{OH})_3$ ,  $\text{MnO}(\text{OH})$ , or  $\text{MnO} \cdot \text{MnO}_2 \cdot (\text{H}_2\text{O})_n$ , or a mixture of all three]. Manganous hydroxide is insoluble in an excess of the precipitant but readily dissolves in a solution of an ammonium salt. (See p. 593.) Colloidal manganese hydroxide (0.25 per cent) in an emulsoind colloid medium is available and recommended in the treatment of acne, boils, furuncles, impetigo, etc.

**Mangano-manganic Oxide** ( $\text{Mn}_3\text{O}_4$ ;  $\text{MnO} \cdot \text{Mn}_2\text{O}_3$ ;  $\text{Mn}_2\text{MnO}_4$ ).—This oxide occurs in Nature as *hausmannite*. It may be made by heating any one of the other oxides of manganese at  $1000^\circ \text{C}$ . for six to eight hours. It is a brownish-black powder which, when

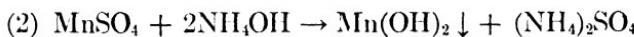
heated with hydrochloric acid, evolves chlorine and forms manganeseous chloride.

**Manganic Oxide** ( $\text{Mn}_2\text{O}_3$ ).—This feebly basic oxide is sometimes called the *sesquioxide*. Hydrated manganic oxide occurs in Nature as *manganite* ( $\text{Mn}_2\text{O}_3 \cdot \text{H}_2\text{O}$ ) and *psilomelane* ( $\text{Mn}_2\text{O}_3 \cdot \text{H}_2\text{O}$ ). It may be prepared as a brownish-black powder by heating manganese dioxide in air for twenty hours at  $700^\circ \text{ C}$ . The hydrated form loses water at  $100^\circ \text{ C}$ , and is converted in hot nitric acid to the soluble nitrate and insoluble manganese dioxide (1).



**Manganic Hydroxide** [ $\text{Mn}_2\text{O}_3 \cdot \text{H}_2\text{O}$ ,  $\text{MnO(OH)}$ ].—This brownish-colored hydroxide is formed when precipitated manganeseous hydroxide is exposed to the air. This compound differs from manganeseous hydroxide by being insoluble in solutions of ammonium salts. It dissolves in cold hydrochloric acid. When this solution is heated, manganeseous chloride is formed and chlorine is evolved.

**Manganese Dioxide** ( $\text{MnO}_2$ ).—This amphoteric compound is by far the most important oxide of manganese. It occurs as such in Nature in the ore *pyrolusite* which is found in large quantities in Russia, Germany, France, the United States, Chile, Cuba, etc. It comes into the trade in black or steel-gray masses, as black amorphous granules, or as a powder. It can be made artificially by the oxidation of manganese oxide with potassium chlorate or nitric acid. A product containing about 80 per cent of  $\text{MnO}_2$ , together with other oxides of manganese, was recognized in the ninth revision of the U. S. Pharmacopœia under the title *Mangani Dioxidum Præcipitatum*. It was prepared by first precipitating manganeseous hydroxide by the action of ammonium hydroxide upon manganese sulfate (2) and then oxidizing the hydroxide at the moment of its formation with hydrogen dioxide (3).



Precipitated manganese dioxide is a very fine, heavy, black powder. It is odorless, tasteless, and permanent in air. It is insoluble in water, in alcohol, in nitric, and in diluted sulfuric acids. When heated with hydrochloric acid, chlorine is evolved and manganeseous chloride formed. (See Weldon Process.) Hot concentrated sulfuric acid acts upon manganese dioxide and oxygen is liberated. When heated to low redness, it gives off one-fourth of its oxygen and is converted into  $\text{Mn}_2\text{O}_3$  and at higher temperatures, it is converted into  $\text{Mn}_3\text{O}_4$ .

With some basic oxides, manganese dioxide forms salts called *manganites* ( $\text{CaMnO}_3$  or  $\text{CaO} \cdot \text{MnO}_2$ ). The manganites are amorphous, brown, water-insoluble solids. They react with hydrochloric acid and chlorine is liberated. Manganese dioxide is of great importance because it is a very powerful oxidizing agent. It is used as a "depolarizer" in electrolytic cells and as a "drier" in paints and

varnishes. Artificially boiled linseed oil often contains manganese dioxide.

Manganese dioxide was thought to possess tonic and alterative properties similar to iron, but at present it is seldom employed. It is sometimes used in 0.25 Gm. (4 grain) doses in the treatment of amenorrhea.

**Manganese Trioxide** (Manganic Anhydride) ( $\text{MnO}_3$ ).—Manganese trioxide is formed as a deliquescent, unstable, red powder when a solution of potassium permanganate in sulfuric acid is dropped upon dry sodium carbonate.<sup>1</sup> It is the anhydride of manganic acid.

**Manganese Heptoxide** (Permanganic Anhydride) ( $\text{Mn}_2\text{O}_7$ ).—Manganese heptoxide is a dark green, oily, very unstable liquid that is strongly acidic. It dissolves in water to form a deep red solution containing *permanganic acid* ( $\text{HMnO}_4$ ). At ordinary temperatures, it continually evolves oxygen and decomposes violently when heated or upon being brought in contact with hydrogen, sulfur, phosphorus, etc. It can be prepared by adding potassium permanganate to well-cooled concentrated sulfuric acid.

**Halogen Compounds.**—**Manganous Chloride** ( $\text{MnCl}_2$ ).—Anhydrous manganous chloride is obtained as a red, crystalline solid by passing hydrogen chloride over manganese carbonate. It has a specific gravity of 2.977 ( $\frac{25}{4}$ ) and melts at  $650^\circ \text{ C}$ . The deliquescent, rose-red tetrahydrate ( $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ ) may be obtained by dissolving manganese or its carbonate in hydrochloric acid and evaporating the solution to crystallization. The crystals have a density of 2.01 and melt at  $58.01^\circ \text{ C}$ . The chloride forms double salts with the alkali chlorides.

*Manganous bromide* ( $\text{MnBr}_2 \cdot 4\text{H}_2\text{O}$ , rose-red), *manganous iodide* ( $\text{MnI}_2 \cdot 4\text{H}_2\text{O}$ , yellowish-brown, deliquescent crystals) and *manganous fluoride* ( $\text{MnF}_2$ , reddish powder) are known.

When manganese dioxide is dissolved in one of the strong halogen acids, the corresponding manganic salt is formed. Manganic tetrachloride ( $\text{MnCl}_4$ ) and the tetrafluoride ( $\text{MnF}_4$ ) are examples.

**Salts of Oxyacids.**—**Manganous Carbonate** ( $\text{MnCO}_3$ ).—Manganous carbonate occurs in Nature as red, trigonal crystals of *rhodochrosite* (impure  $\text{MnCO}_3$ ). A white flocculent precipitate of a hydrated manganese carbonate can be obtained by adding sodium carbonate to a solution of manganous sulfate. Like all of the manganese salts of the weaker acids, it oxidizes readily upon exposure to air to hydrated manganic hydroxide (brown). Sometimes it is used in 0.6 to 2 Gm. (10 to 30 grains) doses in the treatment of anemia.

**Manganous Nitrate** [ $\text{Mn}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ .]—Pink deliquescent crystals of manganous nitrate are made by dissolving manganous carbonate in nitric acid and evaporating the solution to crystallization. The hexahydrate [ $\text{Mn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ ] separates out in long colorless needles which melt at  $25.8^\circ \text{ C}$ . The trihydrate ( $\text{Mn}[\text{NO}_3]_2 \cdot 3\text{H}_2\text{O}$ ) melts at  $34.81^\circ \text{ C}$ .

<sup>1</sup> Franke, B.: J. Prak. Chem., 36, 31 (1887) (2)

**Manganous Phosphate** [Mn<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>.7H<sub>2</sub>O].—Manganous phosphate is a white or pinkish-white powder obtained by adding disodium hydrogen phosphate to a solution of manganous sulfate. It is sometimes used in 1 to 5 grain doses in the treatment of chlorosis.

**Manganous Sulfate** (MnSO<sub>4</sub>).—Manganous sulfate occurs in the form of pale, rose-colored, slightly efflorescent crystals. Depending upon the temperature of the solution, this salt crystallizes with different amounts of water of hydration. The temperature of the solution also affects its crystallographic form. Thus, between 20° and 30° C., rhombic prisms of the tetrahydrate are formed; between 15° and 20° C., the triclinic pentahydrate is produced; whereas below 6° C., a salt having 7 molecules of water of hydration and monoclinic structure is formed. The salt containing 4 molecules of water is soluble in an equal weight of water and forms a neutral solution. It is insoluble in alcohol. With alkali sulfates, manganous sulfate forms double salts.

It is prepared by heating a thick paste of manganese dioxide and concentrated sulfuric acid to dull redness. When white fumes of sulfur trioxide cease to be evolved and when an aqueous solution of a test sample fails to give a test for ferric or ferrous ions, the melt is cooled or crushed and extracted with hot water. This liquid is treated with manganous carbonate to remove traces of iron that have not been rendered insoluble during fusion, again filtered and slowly evaporated to crystallization. A salt that is free from lead, copper, and zinc may be prepared by saturating the solution with hydrogen sulfide, first alone and then in the presence of sodium acetate and acetic acid.

Manganous sulfate is used in the preparation of manganese compounds, in textile dyeing, and in the ceramic industry.

**Manganic Sulfate** [Mn<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>].—Manganic sulfate is a dark green, deliquescent solid. It is decomposed by moist air, heat, and dilute acids. It is prepared by gradually heating a mixture of manganese dioxide and concentrated sulfuric acid to about 140° C. When the material has acquired a dark green color, it is spread on a porous plate. The residue is stirred for some time with nitric acid and, after having been separated from the acid solution, is quickly dried at about 130° C. Manganic sulfate combines with alkali sulfate to form alums, *e. g.*, KMn(SO<sub>4</sub>)<sub>2</sub>.12H<sub>2</sub>O.

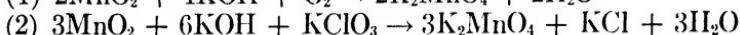
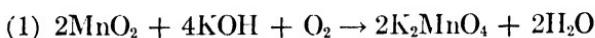
**Sulfides.**—**Manganous Sulfide** (MnS).—Manganous sulfide occurs in Nature as the mineral *alabandite*. It may be made as a green powder by heating the monoxide, sesquioxide or the carbonate in a current of either hydrogen sulfide or carbon disulfide vapors. It can be prepared also by adding an alkali sulfide to a neutral solution of manganous salt. (See p. 594.) The salmon-colored precipitate of hydrated manganous sulfide rapidly absorbs oxygen from the air and turns brown. The precipitate is soluble in dilute acetic acid and in dilute mineral acids.

**Manganese Disulfide** (MnS<sub>2</sub>).—Manganese disulfide occurs in Nature as reddish-brown, cubic crystals of *hauerite*. It may be pre-

pared as a reddish powder by heating manganous sulfate and potassium polysulfide, contained in a sealed tube, to between 160° and 170° C.

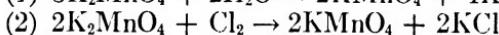
**Manganese Butyrate** [Mn(C<sub>4</sub>H<sub>7</sub>O<sub>2</sub>)<sub>2</sub>].—This is used intramuscularly in the treatment of carbuncles and other skin infections.

**Manganates.**—The manganates are salts of *manganic acid* (H<sub>2</sub>MnO<sub>4</sub>). This acid is unknown in the free state, although its anhydride MnO<sub>3</sub> has been prepared. When an oxide of manganese is fused with an alkali or alkali carbonate, the corresponding manganate is formed (1). The salt can be lixiviated out of the cooled mass and forms a green solution. Potassium chlorate, potassium nitrate or other oxidizing agents are often added to stimulate the reaction (2).



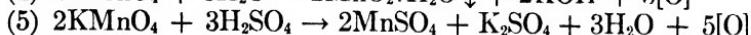
Reducing agents, *e. g.*, sugar, paper, sulfur dioxide, etc., decolorize manganate solutions. The manganates are stable only in alkaline solution. They are employed as oxidizing agents.

**Permanganates.**—The permanganates are salts of *permanganic acid* (HIMnO<sub>4</sub>) which, like manganic acid, is known only in the form of its salts. When a green solution of a manganate is poured into a large volume of water (1) or when it is treated with chlorine (2), bromine, carbon dioxide (3), nitric acid, etc., the color changes to a purplish-red, thus showing the formation of the corresponding permanganate.



Permanganates are made also by the electrolytic oxidation of manganates at the anode.

Potassium and sodium permanganates (KMnO<sub>4</sub>; NaMnO<sub>4</sub>.6H<sub>2</sub>O) are the most important salts. The former occurs in purplish-black, rhombic prisms, which are stable in air. Both salts are very powerful oxidizing agents. In alkaline solution and in the presence of reducing agents, they are first converted into green manganates and then into a brown, hydrated manganese dioxide (4); 2 molecules of the permanganate giving 3 atoms of available oxygen. In acid solution, permanganates are reduced to manganous salts; 2 molecules of the permanganate yielding 5 atoms of oxygen (5).



The alkali permanganates are used as deodorants, disinfectants and as oxidizing agents. They are employed in analytical chemistry, in the synthesis of organic chemicals, in the textile industry, in the cannisters of gas masks, etc.

## IRON, COBALT AND NICKEL

**Introduction.**—Iron, cobalt, and nickel are very definitely magnetic. This property distinguishes them from the other metals.

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### CHAPTER XLIV

#### IRON AND IRON COMPOUNDS

##### IRON

*Iron*, N. F. VIII

*Reduced Iron*, N. F. VIII

Symbol, Fe. Valence, II, III. Atomic Weight, 55.85;  
Atomic Number, 26

**History.**—Iron tools, vessels and ornaments, fashioned by prehistoric man have been found in Egypt. The discovery of iron ore and the development of methods for recovering the metal therefrom exercised a very marked influence on the civilization of a certain early period known as the *Iron Age*. Ancient Persian and Assyrian cuneiform inscriptions show that iron was used by these people. A teacher (Tubal-cain) of workers in iron and copper is mentioned in the Old Testament. The earliest source of iron ores was in India and undoubtedly the Hindus were the first to develop processes for making malleable and wrought iron. Steel was manufactured by the Greeks, and the Chalybes, a people living on the south coast of the Black Sea, were noted for producing high-grade steels. The Romans obtained their iron ore from the Chalybeans and also from Spain, Elba, etc. It is said that the first blast furnace was operated in Germany about 1350 A.D. The symbol Fe is derived from the Latin, *Ferrum*. The name “iron” is derived from the Anglo-Saxon, *isen*.

**Occurrence.**—Metallic iron is found in Nature only in meteorites that have fallen upon the earth. The metal found in meteorites is associated with from 3 to 9 per cent of nickel. With the exception of aluminum, iron in combination occurs more widely distributed and in larger quantities than any other metallic element. It occurs in soil and in small quantities in natural waters and plants (chlorophyll). Iron is a necessary constituent of the blood (hemoglobin) and of the oxidases. It is found in all chromatin and therefore should be found in all cells.

The principal ores of iron consist of the oxides and carbonate. These ores may be reduced by smelting with carbon and yield a metal that invariably contains either free or combined carbon or both, and whose properties are dependent upon the amount of such

carbon present. In the United States (Minnesota) the most important source of iron is the red oxide, *hematite* ( $\text{Fe}_2\text{O}_3$ ). A comparatively small amount of black magnetic oxide of iron, *magnetite* ( $\text{Fe}_3\text{O}_4$ ), is mined in some of the eastern states, but in Norway and Sweden this is the principal iron ore. Germany and France are dependent upon a brown hydrated oxide known as *limonite* ( $2\text{Fe}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ ). An admixture of native ferrous carbonate (*siderite*), clay and shale, known as *iron stone* ( $\text{FeCO}_3$ ) is the chief iron ore of Great Britain. *Iron pyrites*, native iron sulfide and sometimes called "fools' gold," is widely distributed in shining golden yellow crystals. The oxidized residues obtained by roasting this sulfide are not easily reduced and consequently this ore is never worked for iron. It can be used as a source of sulfur dioxide for sulfuric acid manufacture.

**Physical Properties.**—Pure iron is a silvery-white metal having a density of 7.84 to 7.88 and a melting-point of  $1535^\circ \pm 1^\circ \text{ C}$ . It boils at  $3000^\circ \text{ C}$ . It is attracted by a magnet and may be temporarily magnetized. Pure iron is very soft and is not much stronger than lead.

The physical properties of the official forms of metallic iron are as follows:

1. *Iron*.—It is described as elementary iron (Fe) in the form of fine, bright wire, filings or powder. It is almost chemically pure metallic iron and its description is essentially that given above for iron.

2. *Reduced Iron*.—This is an odorless, grayish-black powder, all of which must pass through a No. 100 sieve. It has no luster or not more than a slight luster. If it is examined under a microscope capable of magnifying 100 diameters it appears as an amorphous powder, free from particles having a crystalline structure. It is stable in dry air.

**Chemical Properties.**—The chemical properties of iron will be considered as (1) metallic iron, (2) ferrous ion, and (3) ferric ion.

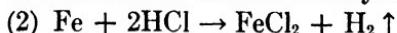
1. The *pure metal* is very active chemically. It burns brilliantly in an atmosphere of oxygen, although *pure* iron is quite resistant to atmospheric oxidation. Rusting of iron is probably due to the presence of impurities in the iron. Carbon dioxide greatly stimulates the formation of hydrated ferric oxide (ferric hydroxide or rust).

Iron combines directly with sulfur to form ferrous sulfide (1).



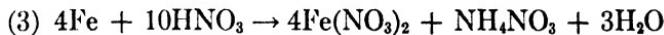
It also reacts more or less readily with the halogens to form first the ferrous halide and then the ferric halide.

Since iron is above hydrogen in the electromotive series it will react with dilute acids to liberate hydrogen and form the corresponding ferrous salt. Hydrochloric acid, for example, dissolves metallic iron to form ferrous chloride and hydrogen (2).

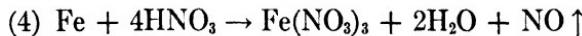


The reaction of nitric acid with iron is dependent upon the concentration of the nitric acid. Dilute nitric acid dissolves iron to

form ferrous nitrate (3), but at the same time reduces the nitrogen of the nitric acid from a valence of 5 to 3.



More concentrated acid causes the formation of ferric nitrate (4).

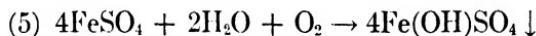


Iron forms two series of salts, the ferrous ( $\text{Fe}^{++}$ ) and the ferric ( $\text{Fe}^{+++}$ ). It forms, however, three oxides,  $\text{FeO}$ ,  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_3\text{O}_4$ .

The last oxide, *magnetite*, is probably ferrous ferrite,  $\text{Fe}\begin{array}{c} \text{O}-\text{Fe}=\text{O} \\ \diagdown \\ \text{O} \end{array}\begin{array}{c} \text{O}-\text{Fe}=\text{O} \\ \diagup \\ \text{O} \end{array}$   
rather than a mixture of  $\text{Fe}_2\text{O}_3$  and  $\text{FeO}$ .

2. *Ferrous salts* are colorless when anhydrous, but when they have water of crystallization they are green in color.

When in the solid state, the ferrous salts are only slowly oxidized by atmospheric oxygen, but when in solution the transformation to the corresponding basic ferric salts (5) is much more rapid.

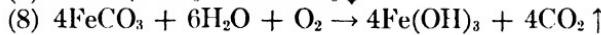


These basic salts are insoluble and usually are brown in color. This accounts for the brown precipitate and scum which slowly form in ferrous sulfate solutions.

Ferrous compounds have a strong tendency to be oxidized to ferric compounds. For this reason they are effective reducing agents. Ferrous sulfate, for example, is readily converted to ferric sulfate by means of nitric acid together with some sulfuric acid to supply sulfate ion (6).



Ferrous ion is readily precipitated from solution by alkali carbonates to form white ferrous carbonate (7), which on contact with air turns green and on further oxidation turns brown due to loss of  $\text{CO}_2$  and consequent formation of ferric hydroxide (8).

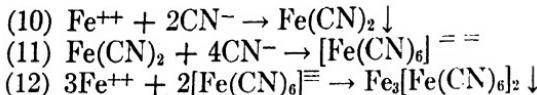


Ferrous ion is also precipitated more or less completely by alkali hydroxides as white ferrous hydroxide (9). Contact with the air, however, converts this rather quickly to brown ferric hydroxide.



Potassium cyanide precipitates ferrous ion as ferrous cyanide (10), the precipitate being soluble in excess potassium cyanide to form potassium ferrocyanide (11). Potassium ferrocyanide is sometimes known as *yellow prussiate of potash* which distinguishes it from *red*

*prussiate of potash* (potassium ferricyanide). Potassium ferricyanide reacts with ferrous ion to form a dark blue precipitate known as Turnbull's blue (12). This reaction is utilized as a sensitive test for ferrous ion, since ferric ion does not react with ferricyanide ion.



3. *Ferric salts* are usually brown or yellow in color with few exceptions. As a rule, they react acidic because of hydrolysis, the hydrolysis being increased with dilution and heating. It follows then that dilution and heating are apt to cause a deposition of basic ferric salts from aqueous solutions (13).

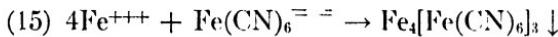


Ammonia and alkali hydroxides precipitate ferric ion as a brown, gelatinous ferric hydroxide (14).



The reaction of ferric ion with thiocyanate ion has been previously discussed (see p. 215).

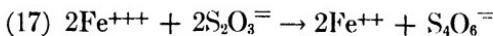
Ferric ion is precipitated as an intense blue precipitate by potassium ferrocyanide (15). This precipitate is known as Prussian blue and is used as a sensitive test for ferric ion.



Sodium phosphate precipitates ferric ion as ferric phosphate especially when sodium acetate is added (16).

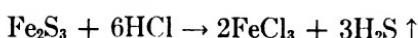
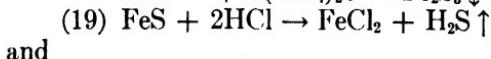
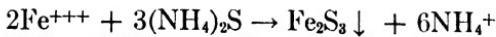
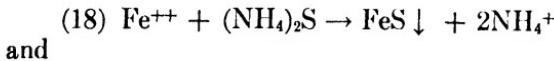


In the presence of sodium thiosulfate, ferric ion in neutral solution is reduced to ferrous ion (17), forming sodium tetrathionate simultaneously.



Ferric salts give dark-colored precipitates with tannins (see p. 620).

**Official Tests for Identity.**—1. Both ferrous and ferric salts yield a black precipitate with ammonium sulfide T.S. (18). This precipitate dissolves completely in cold diluted hydrochloric acid with the evolution of hydrogen sulfide (19).



The official compendia further supplement the sulfide test with specific tests for the two kinds of Fe ions.

(a) *Ferric Salts*.—1. Acid ferric salt solutions give a dark blue precipitate with potassium ferrocyanide T.S. (15).

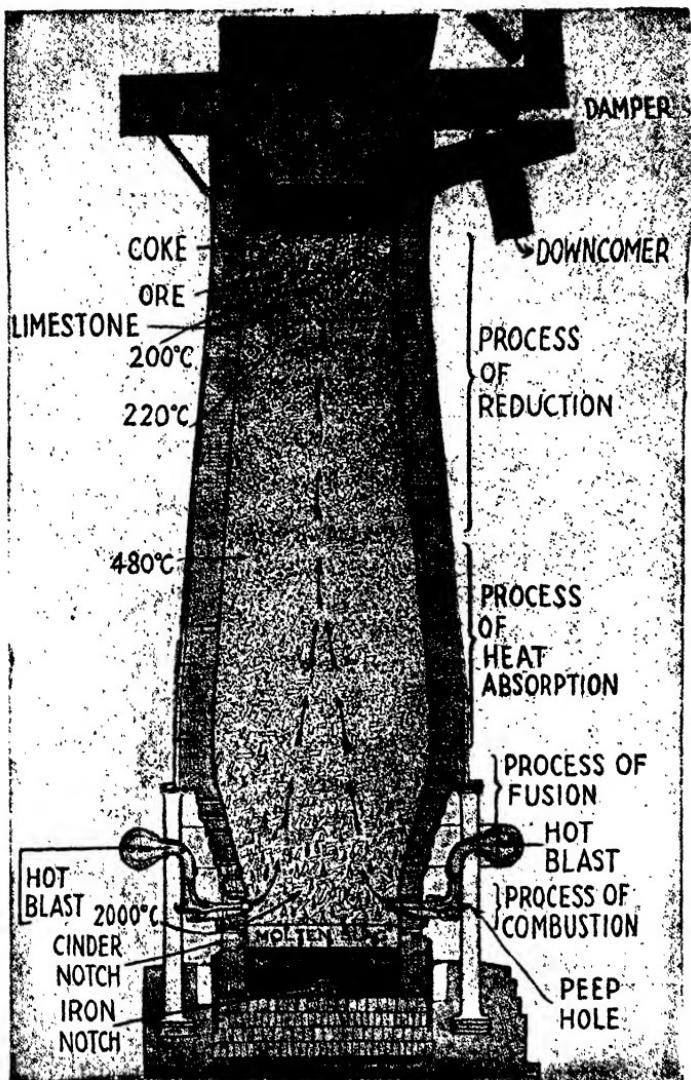


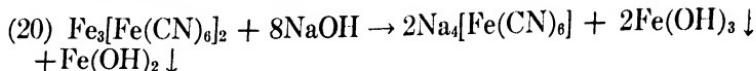
FIG. 24.—Blast furnace. (Courtesy of United States Steel Corporation.)

2. Excess sodium hydroxide T.S. produces a reddish-brown precipitate of ferric hydroxide (14).

3. With ammonium thiocyanate T.S. a deep red color (not destroyed by mineral acids) is formed. (See p. 215.)

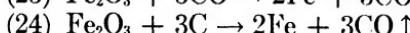
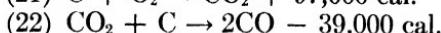
(b) *Ferrous Salts*.—1. Solutions of ferrous salts give a dark blue precipitate with potassium ferricyanide T.S. (12). The precipitate

is insoluble in diluted hydrochloric acid but is decomposed by sodium hydroxide T.S. (20).



2. With ferrous salts sodium hydroxide T.S. forms a greenish-white precipitate (9). The color of this precipitate changes rapidly on shaking to green and then to brown.

**Commercial Manufacture.**<sup>1</sup>—Practically all iron is made from hematite, limonite, or magnetite ores by a process of reduction. This is accomplished by heating the iron ore together with coke and limestone in a blast furnace (Fig. 24). The function of the blast furnace is to (a) reduce the iron oxide to metallic iron, and (b) to remove small quantities of foreign elements (gangue) as slag. The coke indirectly accomplishes the first objective, whereas the limestone does the second. During the smelting of the ore, preheated dry air prepared in blast stoves is forced into the furnace through a set of pipes known as tuyères, thus producing the high temperatures required for the reaction between the ore, coke and limestone. Most of the coke in the lower part of the furnace is converted into carbon dioxide (21). This reaction generates an enormous amount of heat. When the carbon dioxide comes in contact with the slowly settling hot coke, it is almost entirely reduced to carbon monoxide (22), which at the temperature of fusion (1200° to 1600° C.), reduces the iron oxides to metal and is itself oxidized to carbon dioxide (23). The carbon dioxide, in turn, meets the next layer of heated fuel and is changed again to the monoxide. Only a very small amount, if any, of the ore is directly reduced by the hot coke (24). The oxidation of the carbon monoxide to carbon dioxide by the ore (with the setting free of metallic iron) and the reduction of the carbon dioxide to carbon monoxide by the hot coke, continues until the gases, containing about 50 per cent of nitrogen and as much as 20 per cent of carbon monoxide, emerge from the top of the charge and pass into a large pipe (6 to 10 feet in diameter) called the "downcomer." These gases are combustible and are used in the preheaters (blast-furnace stoves) or in operating the compressor engines.



Even the best grades of iron ore contain small quantities of other elements in combination. This *gangue* is composed of silica, manganese oxides, phosphates, sulfur compounds, etc. The temperature at the top of the furnace (300° to 800° C.) is sufficient to convert the limestone (flux) into calcium oxide and carbon dioxide. As

<sup>1</sup> For a more extended discussion of the metallurgy of iron, see the 3rd edition of this textbook.

the quicklime ( $\text{CaO}$ ) settles into the hotter middle zone ( $900^{\circ}$  to  $1200^{\circ}$  C.) of the furnace, it interacts with the alumina and silica to form a fusible slag, which is a mixture of calcium silicate ( $\text{CaSiO}_3$ ) and aluminum silicate [ $\text{Al}_2(\text{SiO}_4)_3$ ]. This slag is tapped off and then is converted into a heavy granular form by running it into water. Slag cinders are sometimes used in the manufacture of cement, paving stones, etc. The smelting converts the other metallic impurities into metals, which either unite or mix with the molten iron.

About every six hours the iron is tapped off into large ladles and transported to casting machines, where the metal is poured into a continuously moving chain of moulds, which overlap slightly on one side. As the metal cools, it is sprayed with lime water to keep it from sticking and, as the moulds reach the pulleys, the "pigs" are dumped directly into cars. At some smelters the molten iron is run into large ladles in which it is transported to another part of the plant where it is made directly into steel.

*Cast Iron.*—The crude metal that is obtained from the blast furnace is called *cast iron* or *pig iron*. It contains from 92 to 94 per cent of iron together with varying quantities of carbon (2.5 per cent), silicon (1 to 3 per cent), manganese (0.7 to 0.9 per cent), phosphorus (0.7 per cent) and sulfur (0.02 to 0.05 per cent), depending upon the character of the ore and coke and also upon the method of operating the furnace. The proportionate amounts of these impurities, together with the rate at which the molten metal is cooled, largely determine the physical properties of iron.

When molten iron is rapidly cooled, the product is a solid solution of hard, brittle iron carbide ( $\text{Fe}_3\text{C}$ ) called *cementite*. This variety is very hard and brittle and is known as *white cast iron*. When the liquid iron is run into sand moulds and allowed to cool slowly, it contains most of its carbon in the form of *graphite scales*. Such a variety is called *gray cast iron* and is much softer and less brittle than the white variety.

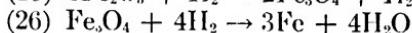
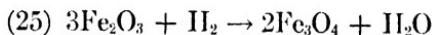
Cast iron has a density of about 7.1 and melts between  $1150^{\circ}$  C. and  $1250^{\circ}$  C. It is not attacked by alkalies and only slightly by concentrated acids. Weak acids dissolve it.

*Wrought Iron.*—Wrought iron is a product obtained by removing most of the impurities from cast iron. It contains from 99.8 to 99.9 per cent of pure iron. It averages about 0.15 per cent of carbon and contains only minute traces of other elements. The micro-structure of wrought iron shows slag fibers and plates and a distinct laminated structure. For this reason, it can be forged when hot, with the slag acting more or less like a lubricant. Wrought iron is very malleable and ductile and can be rolled into sheets or drawn into wire. In these forms the metal is very tough and possesses a high tensile strength. Wrought iron begins to soften at about  $1000^{\circ}$  C., and hence can be forged and welded. It melts at  $1500^{\circ}$  C. and has a density of 7.6 to 7.8. It rusts more rapidly than cast iron and cannot be tempered. At high temperatures it is readily attacked by acids and alkalies.

Wrought iron is made by purifying cast iron in a special type reverberatory furnace. The hearth is made of magnesia and covered with a "felting" of hematite or magnetite. Cast iron is piled on this bed and melted by the flames and hot gases from a fire. The low arched roof deflects the heat down upon the charge. The iron oxides (hematite or magnetite) convert most of the carbon in the cast iron into carbon dioxide, whereas the newly formed oxides of silicon and phosphorus combine with the magnesia lining of the hearth to form a basic slag. The melt is stirred or *puddled* with long iron rods until, with the removal of impurities and the consequent rise in melting-point, it becomes viscid enough to be removed from the furnace in large balls weighing approximately 100 pounds. These balls are called "*blooms*." The blooms are immediately hammered or rolled, which operation squeezes out most of the slag. Newer developments in the manufacture of low-carbon (soft) steels have displaced to a large degree the puddling process described above.

Because of its purity, wrought iron is used to make *crucible steel*. Its properties make it suitable for manufacturing chains, anchors, wire, nails, etc. Because of the purity of this commercial variety of iron, it is recognized under the title *Iron* in the N. F. VIII.

*Reduced Iron*.—This is made by placing dried pure ferric oxide in an iron reduction tube which is so arranged that it may be heated to dull redness during the passage through it of washed (with dilute potassium permanganate) and dried (with concentrated sulfuric acid) hydrogen gas. Between 280° and 300° C., the ferric oxide is changed to the ferroso-ferric oxide ( $\text{Fe}_3\text{O}_4$ ) (25), which at a temperature of 400° C. or above is reduced to metallic iron (26). A bright red heat during the reduction results in a compact, dense product which is undesirable.



As soon as the cessation of water vapor from the tube indicates that reduction is complete, the contents are allowed to cool slowly. A slow current of hydrogen is continued during the cooling in order to prevent the re-oxidation of the iron, which at the high temperature would take place very rapidly in the air. At room temperature, reduced iron is stable.

*Steel*.—This commercial variety of iron may be characterized as one that contains carbon in definitely known amounts with almost no silicon, phosphorus or sulfur. There are many kinds of steel, each one of which possesses definite and known properties that have been imparted to it through the several processes of manufacture, by special operations or by added constituents. For example, low-carbon steels are soft and ductile and can be forged and welded, whereas the higher carbon steels are harder, more tenacious, and can be tempered. A very hard and brittle steel can be made by heating a high carbon steel (0.75 to 1.5 per cent) to about 800° C. and then suddenly plunging it into cold water or oil. When the

very hard product is reheated and allowed to cool slowly, a steel that is less hard and brittle is obtained. A steel having nearly any degree of hardness and brittleness may be obtained by varying the carbon content and the heat treatment (*tempering*). Steels, to which other metals have been added, are no longer *simple steels*, but rather, *true alloys*. The properties of these alloys are due not only to their chemical composition but also to the heat treatment which they receive.

**Pharmacological Action of Iron and Its Salts.**—The role of iron in the body economy has been the subject of much and varied research. It is, of course, well established that iron forms an essential part of the hemoglobin in the blood. Also, much evidence has been accumulated to show that traces of iron in the blood and tissues play a significant part in the oxidation-reduction reactions constantly taking place in normal metabolism.

Viewed from a medicinal standpoint, iron and its preparations fall into two classifications, (1) those used *externally*, and (2) those used *internally*.

1. *External* iron preparations are almost exclusively of the ferric type, and depend for their action principally on their ability to precipitate protein. This ability to precipitate protein is directly reflected in the fact that ferric salts when used externally are astringents. The astringent action is of value in stopping the bleeding of small cuts, in gargles, etc. One of the disadvantages of iron is that it is colored, whereas lead, for example, is colorless.

The use of ferric chloride solution as an application to the skin in cases of poison ivy poisoning is based largely on the ability of ferric salts to precipitate phenols, vesicant phenols being the causative agent in poison ivy poisoning. This phenol-precipitating power combined with the potential oxidizing properties of the ferric ion on the sensitive phenols was probably the rationale for the introduction of iron into poison ivy therapy. Research has shown,<sup>1</sup> however, that the iron-phenol precipitate is still an exceedingly active irritant to the skin. This tends to prove that the use of ferric chloride (the ferric salt most commonly used) in poison ivy treatment is without sound scientific background.

2. *Internal* iron preparations are used mostly for their ability to cause increased formation of hemoglobin. For this purpose iron can be used therapeutically in one or all of three forms: (a) metallic iron, (b) ferric salts, (c) ferrous salts.

Each of these basic forms of iron has been used in the regeneration of hemoglobin with some success. However, it is well to note that the actual per cent of iron in a preparation or salt has no bearing on the amount which will be absorbed and ultimately be effective. For example, metallic iron has by far the greatest content of iron on a percentage basis but weight for weight is inferior in hematitic activity to ferrous sulfate with much less iron. The effectiveness of iron preparations is thought to be a function of the extent to which

<sup>1</sup> Gisvold, O.: J. Am. Pharm. Assn., Sc. Ed., 30, 17 (1941). See also this book.

ferrous iron is liberated and absorbed as a result of gastric and intestinal secretions. The preceding statement is borne out by much research and clinical observation, all of which show that the administration of ferrous salts results in greater hemoglobin response than that obtained with any other form of iron. The low order of activity associated with ferric iron is at least partly due to its tendency to form insoluble compounds with phosphates, carbonates and proteins; this even in the normally acid medium of the stomach. Ferrous salts do not precipitate in this manner unless in an alkaline medium. Since the normal stomach reaction is acid there is little possibility of inactivating ferrous iron. Assuming that ferrous salts are the most advantageous form in which to administer iron, it only remains to determine the most suitable anion to accompany it. Experience has indicated that the sulfate is fairly stable and that in most cases it does not cause any marked gastric upset. However, there is a small percentage of patients who do get a *gastro-enteritis* from the use of ferrous sulfate. This may be avoided in some cases by the administration of the ferrous sulfate in an enteric coated tablet, whereas others require changing the salt. In the case of the latter, the use of ferrous gluconate has met with pronounced success. As an illustration, a patient who could not tolerate 35 mg. of iron per day in the form of ferrous sulfate was shifted to ferrous gluconate. By gradually increasing the dose, the patient was able to take 108 mg. of iron (0.9 Gm. of ferrous gluconate) without discomfort. By and large, however, ferrous sulfate is probably the most economical and most satisfactory form of ferrous iron on the market today.

The use of copper in small amounts along with iron is based upon experimental evidence (see p. 282), which shows that iron is better absorbed when accompanied by copper. There is also some evidence to show that molybdenum (as oxide) also potentiates the absorption of iron.

Parenteral forms of iron have not been well received, partly because they often cause marked local and systemic reactions and also because transfusions in most cases will serve just as well.

The chief indication for the use of iron salts is in the treatment of so-called "secondary anemias." The derivation of the terminology "secondary" is due to the fact that these iron-deficiency diseases are secondary to some other disease, that is, a result of another disease. Any and all disease conditions which can affect the body may, and most of them do, ultimately lead to a secondary anemia, which is characterized by a hemoglobin which is low in proportion to the decrease in the number of red blood cells. These secondary anemias are also classified as "hypochromic microcytic anemias" indicating a low hemoglobin content and small size cells. Some of the disease conditions which cause this type of anemia are bleeding peptic ulcer, ulcerative colitis, tuberculosis, etc. Iron is indicated in all of these secondary anemias, although sometimes liver in one form or another is administered simultaneously.

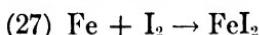
In contrast to the secondary anemias we have the so-called "primary anemias" which are typified by pernicious anemia. They are also called "macrocytic anemias" to indicate that the blood cells are larger than normal. The blood picture in the primary anemia group shows that the cells are normally colored but are of a larger size than normal. These anemias are not secondary to some other disease but are due to a diseased condition of the blood-making portions of the body. They are treated with liver extract or other similar preparations. Iron is of little value in this type of anemia.

**Pharmaceutical Preparations and Uses.**—1. *Iron* (Ferrum), N. F. VIII.—"Elementary Iron (Fe) in the form of fine, bright wire, filings or powder." This form of iron is officially identified by its solubility in hydrochloric acid with evolution of hydrogen, the solution corresponding to tests for *Ferrous Salts*. This form of iron is used mostly for preparing certain iron salts, *e. g.*, ferrous iodide, ferrous chloride, etc.

2. *Reduced Iron* (Ferrum Reductum, Iron by Hydrogen), N. F. VIII.—"Reduced iron is obtained by the action of hydrogen upon ferric oxide and contains not less than 90 per cent of Fe." This form of iron is identified by the fact that if heated to a blue-black color in a crucible and then quickly poured from the crucible, the particles of iron will glow as they fall through the air. This form of iron is used for internal administration to obtain the hematinic effects of iron. It is probably converted in part to ferrous chloride in the acid stomach juices and as such exerts its effect. Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains).

3. *Reduced Iron Capsules* (Capsulae Ferri Reducti), N. F. VIII.—These capsules "contain an amount of metallic iron (Fe) corresponding to not less than 86 per cent and not more than 102 per cent of the labeled amount of Fe." Average dose—0.5 Gm. (approximately  $7\frac{1}{2}$  grains) of Reduced Iron.

*Ferrous Iodide Syrup* (Syrupus Ferri Iodidi, Sirupus ferrois iodidi concentratus P. I.), N. F. VIII.—This syrup contains "in each 100 cc., not less than 6.5 Gm. and not more than 7.5 Gm. of  $\text{FeI}_2$ , representing approximately 5 per cent of  $\text{FeI}_2$ , by weight." It may be prepared by reacting iron (in the form of fine, bright wire) with iodine (27) to form ferrous iodide. The ferrous iodide formed is protected from oxidation by the addition of a small



amount of hypophosphorous acid. The fact that it is in a syrup made with sucrose also tends to inhibit oxidation. To further retard discoloration, which is due to unstable fructose formation by inversion of the sucrose by the hypophosphorous acid, the N. F. VIII permits the hypophosphorous acid to be replaced by 1.3 Gm. of citric acid. This preparation is often made in the pharmacy from commercial ampuls which contain an amount of an aqueous solution of ferrous iodide sufficient to make a designated quantity

of the syrup. The contents of an ampul may be added to syrup at any desired time to give a freshly made syrup. Syrup of Ferrous Iodide is a hematinic preparation. Average dose—1 cc. (approximately 15 minims).

### OFFICIAL IRON COMPOUNDS

#### FERRIC AMMONIUM CITRATE

*Ferric Ammonium Citrate*, U. S. P. XIII

Formula, Indefinite

**Physical Properties.**—Ferric Ammonium Citrate occurs in thin, transparent scales which are garnet-red in color and odorless. It also occurs as granules or as a brownish powder. It deliquesces in air and is affected by light.

It is very soluble in water, the solutions having a saline, mildly ferruginous taste. Aqueous solutions are neutral or only faintly acid or alkaline in reaction. It is insoluble in alcohol.

**Chemical Properties.**—Although this preparation contains the ferric form of iron, it does not exhibit the normal reactions of that ion when in solution. For example, it does not precipitate with ammonium hydroxide, it fails to precipitate protein and it does not react with potassium ferrocyanide. It is only after acidification with hydrochloric acid that it is possible to get the normal reactions of ferric ion.

The chemistry of ferric ammonium citrate has received much attention, but an exact explanation is still to be had. It is claimed by some that the preparation actually is a true salt having the formula  $(\text{NH}_4)_3\text{Fe}(\text{C}_6\text{H}_5\text{O}_7)_2$ . Still others claim that it is a solid sol of a basic colloid complex,  $\text{FeC}_6\text{H}_5\text{O}_7 \cdot 2\text{Fe(OH)}_3$ , dispersed in ammonium citrate. Thus, little is to be gained by attempting to correlate the widely divergent views upon the chemistry of this common pharmaceutical preparation.

**Official Tests for Identity.**—1. When strongly heated, this preparation chars and finally leaves a residue of ferric oxide. This is characteristic of all metallic salts of organic acids.

2. When ammonia T.S. is added to 1 in 100 solution of Ferric Ammonium Citrate in water, there is no precipitation, but there is a darkening of the solution.

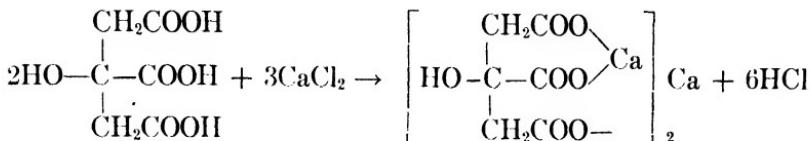
3. Five cc. of a 1 in 100 aqueous solution of the preparation is treated with 0.3 cc. of potassium permanganate T.S. and 4 cc. of mercuric sulfate T.S. and heated to boiling. A white precipitate is formed.

4. The iron is removed from 10 cc. of a solution of Ferric Ammonium Citrate (1 in 10) by boiling it with sodium hydroxide T.S. (1)

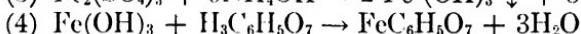
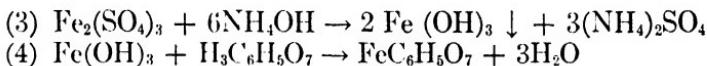


The filtrate from this precipitate is made slightly acid with acetic acid and upon the addition of calcium chloride T.S. and boiling, a white crystalline precipitate of calcium citrate forms (2).

(2)



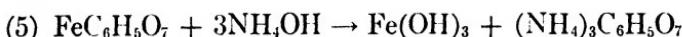
**Commercial Manufacture.**—This preparation is made by adding ammonium hydroxide in slight excess to a solution of ferric citrate, which previously has been made by dissolving freshly precipitated ferric hydroxide in a solution of citric acid. The reaction involved in the preparation of ferric hydroxide is typified by the use of ferric sulfate as a source of ferric ion (3). To this freshly prepared magma (free of sulfate) is then added the citric acid, and although this reaction may not be in accord with all experimental facts it, nevertheless, gives a working equation (4).



Addition of ammonium hydroxide to the ferric citrate then gives a solution which is evaporated to a syrup, spread on glass plates, and "scaled." Scaling is a pharmaceutical process whereby a syrup which is thinly spread on glass plates loses water by evaporation. When sufficient water has evaporated the residue begins to break away from the glass plate in the form of scales. These scales are not crystalline, although sometimes they may appear to be.

In the case of ferric ammonium citrate, for purposes of yield calculation, one could consider that a reaction takes place between ammonium hydroxide and ferric citrate (5).

This equation does not accurately represent, perhaps, the actual reaction, but at least it can be said that the sum total of materials that go into the making of the preparation should appear in the finished product and this affords a means of calculating the yield. It might be added, however, that the per cent of retained water in the preparation in a scaled form is variable and this will make it appear as though a greater yield has been obtained than is actually the case.



**Pharmaceutical Preparations and Uses.**—1. *Ferric Ammonium Citrate* (Ferri Ammonii Citras, Iron and Ammonium Citrates, U. S. P. XII), U. S. P. XIII.—"Ferric Ammonium Citrate contains ferric citrate equivalent to not less than 16.5 per cent and not more than 18.5 per cent of Fe." This scale salt of iron has been used as a convenient source of iron for hematinic purposes. Because of its solubility, it lends itself very nicely to incorporation into

syrups, elixirs, etc. Its chief disadvantage lies in the fact that it requires quite large doses to produce the hematinic action. As a comparison, it is only one-eighth as effective as an equal weight of exsiccated ferrous sulfate. Average dose—1 Gm. (approximately 15 grains).

2. *Ferric Ammonium Citrate Capsules* (*Capsulae Ferri Ammonii Citratis, Iron and Ammonium Citrates Capsules, U. S. P. XII*), *U. S. P. XIII.*—These capsules "contain an amount of iron (Fe) corresponding to not less than 15.5 per cent and not more than 19.5 per cent of the labeled amount of ferric ammonium citrate." They are a convenient means of administering this preparation orally. These capsules are usually marketed in  $7\frac{1}{2}$ -grain size. Average dose of *Ferric Ammonium Citrate*—1 Gm. (approximately 15 grains).

3. *Beef, Iron and Wine* (*Caro, Ferrum et Vinum*), *N. F. VIII.*—This preparation "contains, in each 100 cc., an amount of ferric ammonium citrate corresponding to not less than 0.75 Gm. and not more than 0.975 Gm. of Fe." It is prepared by dissolving a specified amount of beef extract in distilled water and adding compound orange spirit, alcohol and syrup to this solution. Then the ferric ammonium citrate is dissolved in sherry wine and added to the solution previously made. After rendering the resulting product neutral or slightly alkaline to litmus by the addition of diluted ammonia solution, enough sherry wine is added to make the mixture measure 1000 cc. It is then allowed to stand for two days and filtered. This preparation contains the ferric ammonium citrate as a hematinic. The preparation is used as a tonic. Average dose—8 cc. (approximately 2 fluidrachms).

### GREEN FERRIC AMMONIUM CITRATE

#### *Green Ferric Ammonium Citrate, N. F. VIII*

##### Formula, Indefinite

**Physical Properties.**—This preparation occurs in the form of thin, transparent scales, granules, or as a powder. It is green in color. It deliquesces in air and is affected by light. It dissolves very readily in water to give solutions which are acid to litmus. The preparation is odorless and has a saline, mildly ferruginous taste. It is insoluble in alcohol.

**Chemical Properties.**—The properties of this preparation are very similar to those of the closely related ferric ammonium citrate. The principal difference is that this preparation contains slightly less iron on a per cent basis.

**Official Tests for Identity.**—1. Heating the material with potassium hydroxide T.S. results in the formation of a precipitate of ferric hydroxide.

2. Addition of ammonia T.S. produces no precipitate but changes

the yellow-green color of its solutions to orange or reddish-brown. The color deepens upon standing.

3. Addition of mercuric sulfate T.S. and potassium permanganate T.S. to a 1 in 100 solution together with boiling causes the formation of a white precipitate.

4. When the iron is removed from a solution (1 in 10) of the preparation by boiling with potassium hydroxide T.S., the filtrate gives the characteristic test (see p. 182) for citric acid when it is slightly acidified with acetic acid.

**Commercial Manufacture.**—It is made in exactly the same manner as Ferric Ammonium Citrate (see p. 615). However, it does contain more ammonium citrate (approximately 8 per cent).

**Pharmaceutical Preparations and Uses.**—1. *Green Ferric Ammonium Citrate* (Ferri Ammonii Citras Viridis), N. F. VIII.—“Green Ferric Ammonium Citrate contains ferric citrate equivalent to not less than 14.5 per cent and not more than 16 per cent of Fe.” This preparation has an advantage over Ferric Ammonium Citrate in that it may be injected intramuscularly without as much irritation. Although injections of even this preparation are quite painful, it is probably the iron preparation of choice for parenteral use. As pointed out previously, iron is seldom administered parenterally. Average dose--intramuscular, 0.1 Gm. (approximately 1½ grains).

2. *Green Ferric Ammonium Citrate Ampuls* (Ampullæ Ferri Ammonii Citratis Viridis, Green Ferric Ammonium Citrate Injection), N. F. VIII.—These ampuls “contain a sterile solution of green ferric ammonium citrate, and may contain 0.5 per cent of quinine and urea hydrochloride, in water for injection, and yield Fe, equal to not less than 14.5 per cent and not more than 16 per cent of the labeled amount of green ferric ammonium citrate.” Average dose—0.1 Gm. of Green Ferric Ammonium Citrate.

## FERRIC CACODYLATE

### *Ferric Cacodylate*, N. F. VIII

Formula,  $\text{Fe}[(\text{CH}_3)_2\text{AsO}_2]_3$ . Molecular Weight, 466.78

**Physical Properties.**--This salt occurs as a yellowish, amorphous powder. One Gm. is soluble in about 30 cc. of water at 25° C. It is only slightly soluble in alcohol.

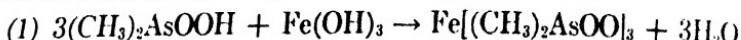
**Chemical Properties.**—The chemical properties of this compound are essentially those of the ferric ion (*q. v.*) and of the cacodylate ion (*q. v.*).

**Official Tests for Identity.**—1. Ferric Cacodylate emits the odor of garlic when burned. It burns with a blue flame.

2. When a few drops of a 1 in 100 solution is allowed to stand in contact with 2 cc. of hypophosphorous acid in a closed tube, the mixture develops the odor of cacodyl within one hour.

**Commercial Manufacture.**—Details of the manufacture of ferric cacodylate are difficult to find. However, the probable method of

manufacture is by reacting cacodylic acid, which is made from arsenic trioxide (see p. 528), with ferric hydroxide (1).



**Pharmaceutical Preparations and Uses.**—1. *Ferric Cacodylate* (Ferri Cacodylas, Iron Cacodylate), N. F. VIII.—“Ferric Cacodylate, when dried to constant weight at 105°, contains not less than 11 per cent and not more than 16 per cent of Fe, and not less than 41 per cent and not more than 45 per cent of As.” This salt is used in treating anemias which require both iron and arsenic. It is also said to be of value in leukemia. The cacodylate portion of the molecule liberates its arsenic slowly, but it behaves therapeutically as an inorganic arsenical. Ferric cacodylate is administered intramuscularly or in some cases intravenously. The usual dose is  $\frac{1}{2}$  to 1 grain every two to five days. Average dose—60 mg. (approximately 1 grain).

2. *Ferric Cacodylate Ampuls* (Ampullae Ferri Cacodylatis, Iron Cacodylate Ampuls, Ferric Cacodylate Injection), N. F. VIII.—These ampuls “contain a sterile solution of ferric cacodylate in water for injection, and yield As equal to not less than 38.7 per cent and not more than 47.3 per cent of the labeled amount of  $\text{Fe}[(\text{CH}_3)_2\text{AsO}_2]_3$ .” The ampuls commercially supplied are of 1 cc. size containing  $\frac{1}{2}$  grain per cc., or may also be obtained as 5 cc. ampuls containing 1 grain per ampul. Average dose—60 mg. of Ferric Cacodylate.

### FERRIC CHLORIDE

Formula,  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ . Molecular Weight, 270.30

*Note.*—This compound is not official, but there are several official preparations in which it occurs. Therefore, it will be discussed with the official compounds.

**Physical Properties.**—This compound occurs as very deliquescent, crystalline lumps having a brownish-yellow to orange color. Ordinarily, they have an odor of hydrochloric acid. It is affected by light.

One Gm. dissolves in 0.25 cc. of water, and in 1.2 cc. of alcohol. It is freely soluble in acetone. It is also soluble in ether or glycerin. Aqueous solutions of the salt have an acid reaction.

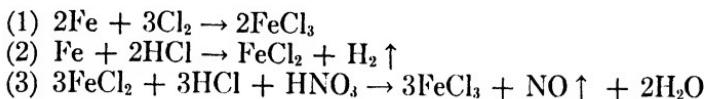
**Chemical Properties.**—This salt gives an acid reaction in aqueous solution because of hydrolysis. This has been shown to be characteristic of ferric salts. In its reactions ferric chloride exhibits those of the ferric ion and of the chloride ion.

**Tests for Identity.**—Since ferric chloride itself is not official it has no “official” tests for identity. However, Ferric Chloride Solution is official and has official tests for identity.

1. A 1 in 10 aqueous dilution of Ferric Chloride Solution responds to all tests for ferric ion (*q. v.*) and for chloride ion (*q. v.*).

**Commercial Preparation.**—Ferric chloride may be prepared either by heating iron in a current of chlorine (1) or by oxidizing a solution

of ferrous chloride (obtained by dissolving iron in hydrochloric acid) (2) with nitric acid (3).



Reaction (1) produces an anhydrous form of ferric chloride which exists as dark green crystals having a metallic luster. This form is quite volatile. Once it is dissolved in water, or if the ferric chloride is made by reactions (2) and (3) it is no longer possible to get back the anhydrous form. When an aqueous solution of ferric chloride is evaporated, several different hydrates may be formed. Usually the hexahydrate is the one that is isolated. If one attempts to drive off all of the water, the concentrated material evolves hydrogen chloride fumes and eventually leaves behind a residue of ferric oxide.

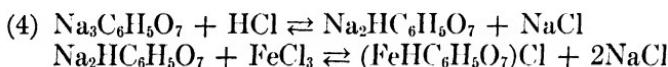
**Pharmaceutical Preparations and Uses.**—1. *Ferric Chloride Solution* (Liquor Ferri Chloridi, Iron Perchloride Solution), N. F. VIII.—This preparation "is an aqueous solution containing ferric chloride ( $\text{FeCl}_3$ ), corresponding to not less than 10 per cent and not more than 11 per cent of Fe, and not less than 3 per cent and not more than 5 per cent of HCl." It is a yellowish-orange liquid having a faint odor of hydrochloric acid and an acid reaction to litmus. This solution is used principally for making *Ferric Chloride Tincture*, N. F. VIII and *Ferric Citrochloride Tincture*, N. F. VIII. However, it may be used externally for the astringent and styptic effect of the ferric ion. In a diluted form or in one of the above tinctures, it may be used as a hematinic, although there are other preparations much more satisfactory. Average dose—0.1 cc. (approximately  $1\frac{1}{2}$  minimis).

2. *Ferric Chloride Tincture* (Tinctura Ferri Chloridi, Iron Tincture), N. F. VIII.—This "is a hydro-alcohol solution containing, in each 100 cc., about 13 Gm. of  $\text{FeCl}_3$ , corresponding to not less than 4.5 Gm. of Fe." It is prepared by mixing 350 cc. of Ferric Chloride Solution with enough alcohol to make 1000 cc. of finished product. It is used externally as a styptic and astringent, and internally as a hematinic and tonic. Average dose—0.6 cc. (approximately 10 minimis).

3. *Ferric Citrochloride Tincture* (Tinctura Ferri Citrochloridi), N. F. VIII.—This "is a hydro-alcohol solution containing, in each 100 cc., ferric citrochloride equivalent to not less than 4.48 Gm. of Fe." It is prepared by mixing 350 cc. of Ferric Chloride Solution with 150 cc. of water and dissolving the sodium citrate in this mixture with the aid of gentle heat. Alcohol (150 cc.) is added when cool. The mixture is then made up to 1000 cc. with water and allowed to stand in a cold place for a few days to let excess saline matter ( $\text{NaCl}$ , which is insoluble in alcohol) settle out. It is then filtered.

The reactions taking place in this preparation are not definitely

known, although some have been postulated (4). Whatever they may be, the brown color of the Ferric Chloride Solution is changed to a green color. Accompanying this color change is a change in the chemical reactivity of the iron which is present. The iron is apparently bound up in an undissociated form since it no longer gives the reactions of ferric ion, and has lost its astringent and styptic properties. This tincture is, therefore, unsuited for astringent use, but is used internally as a hematinic, since it lacks many of the objectionable qualities associated with Ferric Chloride Tincture. In addition, it is of service in avoiding many of the incompatibilities associated with Tincture of Ferric Chloride, such as the dark colored precipitate which iron in an ionized form gives with tannins, etc. Average dose—0.5 cc. (approximately 8 minims).



4. *Iron and Ammonium Acetate Solution* (Liquor Ferri et Ammonii Acetatis, Basham's Mixture), N. F. VIII.—This solution "yields, from each 100 cc., not less than 0.16 Gm. and not more than 0.2 Gm. of Fe, and not less than 0.6 Gm. and not more than 0.8 Gm. of NH<sub>3</sub>." It is made by adding to ammonium acetate solution (see p. 270), diluted acetic acid, ferric chloride tincture, aromatic elixir and glycerin. The solution is finally brought to volume with distilled water.

5. *Iron, Quinine and Strychnine Elixir* (Elixir Ferri, Quininæ et Strychninæ, Elixir I. Q. & S.), N. F. VIII.—This elixir contains ferric citrochloride tincture together with quinine hydrochloride, strychnine sulfate, compound orange spirit, alcohol, glycerin and sufficient distilled water to bring it to volume. This is a tonic preparation with some hematinic properties. Average dose—4 cc. (approximately 1 fluidrachm).

### FERRIC GLYCEROPHOSPHATE

#### *Ferric Glycerophosphate*, N. F. VIII

Formula, Fe<sub>2</sub>[C<sub>3</sub>H<sub>5</sub>(OH)<sub>2</sub>PO<sub>4</sub>]<sub>3</sub>. Molecular Weight, 621.90

**Physical Properties.**—This salt occurs as orange- to greenish-yellow, transparent, amorphous scales, or powder. It is odorless, and nearly tasteless. It is affected by light.

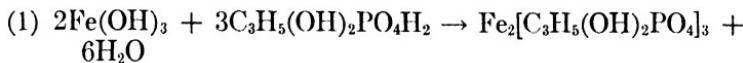
One Gm. dissolves slowly in about 2 cc. of water at 25° C. It is insoluble in alcohol.

**Chemical Properties.**—Due to hydrolysis, aqueous solutions of ferric glycerophosphate are acidic in reaction. The reactions of this salt when in aqueous solution are essentially those of the ferric ion (*q. v.*) and of the glycerophosphate ion (*q. v.*).

**Official Tests for Identity.**—1. A 1 in 20 aqueous solution responds to the tests for *Ferric Salts* (*q. v.*).

2. A 1 in 20 aqueous solution also responds to all tests for *Glycerophosphate* ion (*q. v.*).

**Commercial Manufacture.**—Ferric Glycerophosphate is made by dissolving freshly precipitated ferric hydroxide in glycerophosphoric acid (1) and concentrating the liquid to a syrupy consistency in a vacuum. It is then spread on glass plates, dried and scaled.



**Pharmaceutical Preparations and Uses.**—1. *Ferric Glycerophosphate* (Ferri Glycerophosphas), N. F. VIII.—“Ferric Glycerophosphate, when dried to constant weight at 130°, contains not less than 17 per cent of Fe, corresponding to not less than 95 per cent of  $\text{Fe}_2[\text{C}_3\text{H}_5(\text{OH})_2\text{PO}_4]_3$ . This salt is used for much the same purpose as calcium glycerophosphate, but has added hematinic properties. Average dose—0.2 Gm. (approximately 3 grains).

2. *Compound Glycerophosphates Elixir* (Elixir Glycerophosphatum Compositum, Compound Glycerophosphates Solution), N. F. VIII.—This elixir contains 3 Gm. of ferric glycerophosphate per 1000 cc. of finished elixir. It also contains other glycerophosphates (Na, Ca and Mn) in varying quantities together with strychnine nitrate, citric acid, lactic acid, compound cardamom spirit, alcohol, glycerin and distilled water. (See also p. 188.) Average dose—8 cc. (approximately 2 fluidrachms).

## FERRIC HYPOPHOSPHITE

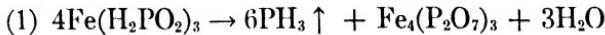
### *Ferric Hypophosphite*, N. F. VIII

Formula,  $\text{Fe}(\text{H}_2\text{PO}_2)_3$ . Molecular Weight, 250.84

**Physical Properties.**—Ferric Hypophosphite is a white or grayish-white powder. It is odorless and nearly tasteless. It is stable in air.

One Gm. of the salt is soluble in about 2300 cc. of water at 25° C., and in about 1200 cc. of boiling water. Hypophosphorous acid increases its solubility. It dissolves readily in a warm, concentrated solution of an alkali citrate to form a green solution. It is soluble in hydrochloric acid.

**Chemical Properties.**—When strongly heated, ferric hypophosphite decomposes into poisonous phosphine and ferric pyrophosphate (1).



The solubility of ferric hypophosphite in acids such as acetic and hydrochloric is probably due to the formation of the corresponding ferric salt (2) together with hypophosphorous acid.



When thus solubilized it gives the reactions of the ferric ion and also of the hypophosphite ion.

Because of its low solubility this salt enters into few reactions.

**Official Tests for Identity.**—1. When 1 Gm. of the salt is dissolved in 15 cc. of acetic acid by boiling, the filtrate responds to the tests for *Ferric Salts* (*q. v.*).

2. The filtrate also responds to the tests for *Hypophosphite* ion.

**Commercial Manufacture.**—This salt can be prepared by gradually adding a solution of ferric chloride to a solution of calcium hypophosphite (3). The mixture is allowed to stand for about three days and the precipitate washed entirely free from calcium chloride and dried.



It may be prepared also by dissolving ferric hydroxide in hypophosphorous acid, concentrating the solution, and "sealing."

**Pharmaceutical Preparations and Uses.**—1. *Ferric Hypophosphite* (*Ferri Hypophosphis*), N. F. VIII.—"Ferric Hypophosphite, when dried to constant weight over sulfuric acid, contains not less than 21.8 per cent of Fe, corresponding to not less than 98 per cent of  $\text{Fe}(\text{H}_2\text{PO}_2)_3$ ." The N. F. VIII also states: Caution should be observed in compounding Ferric Hypophosphite with other substances, as an explosion may occur if it is triturated or heated with nitrates, chlorates or other oxidizing agents. Ferric hypophosphite is used as a hematinic. Average dose—0.2 Gm. (approximately 3 grains).

2. *Compound Hypophosphites Syrup* (*Syrupus Hypophosphitum Compositus*), N. F. VIII.—This syrup contains 2.2 Gm. of ferric hypophosphite per 1000 cc. of finished preparation. It also contains other hypophosphites (Ca, K, Na and Mn) in varying quantities together with strychnine, sodium citrate, hypophosphorous acid, dextrose, glycerin and distilled water. The purpose of the sodium citrate in this preparation is to solubilize the somewhat insoluble ferric and manganese hypophosphites. (See also p. 197.) Average dose—8 cc. (approximately 2 fluidrachms).

### RED FERRIC OXIDE

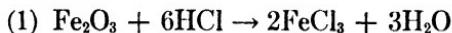
#### *Red Ferric Oxide*, N. F. VIII

Formula,  $\text{Fe}_2\text{O}_3$ . Molecular Weight, 159.70

**Physical Properties.**—This oxide occurs as a moderate reddish-brown powder which closely approximates the color of a mixture of 1 part scarlet-red, and 18 parts red mercuric oxide.

It is insoluble in water and organic solvents. It is soluble in hydrochloric acid with warming, usually leaving a small residue.

**Chemical Properties.**—This oxide dissolves in hydrochloric acid as mentioned previously (1).



Because of its insolubility this oxide enters into few reactions other than those with acids.

**Official Tests for Identity.**—The N. F. VIII does not provide specific tests for identity, but identification can be obtained through a consideration of its physical and chemical properties.

**Commercial Manufacture.**—Red ferric oxide occurs naturally as *red hematite* ore ( $\text{Fe}_2\text{O}_3$ ) which is powdered to the required state of fineness. Red forms of ferric oxide can also be made synthetically, *e. g.*, by the reduction of magnetite ( $\text{Fe}_3\text{O}_4$ ) which gives *Venetian red*, a desirable pigment for paints. Artificial preparation of ferric oxide by heating ferric hydroxide, nitrate or sulfate results in a steel-gray powder rather than in a red powder.

Yellow ferric oxide occurs naturally as a hydrated ferric oxide. Its most common form of occurrence is as *limonite* ( $2\text{Fe}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ ) which ranges in color from yellow to brown. Some samples of limonite may be obtained which have practically the same color as that required by the N. F. VIII. Other naturally occurring hydrated ferric oxides are *goethite* and *lepidocrocite*, both having the formula,  $\text{Fe}_2\text{O}_3 \cdot \text{H}_2\text{O}$ .

A very fine ferric oxide is used for polishing metals and is known as "*jeweler's rouge*."

**Pharmaceutical Preparations and Uses.**—1. *Red Ferric Oxide* (Ferri Oxidum Rubrum), N. F. VIII.—"Red Ferric Oxide contains not less than 90 per cent of  $\text{Fe}_2\text{O}_3$  calculated on the basis of the ignited product, the loss on ignition being determined on a separate sample." The reason for the introduction of this oxide of iron (together with *Yellow Ferric Oxide*) was to provide coloring materials for preparations designed for application to the skin. No therapeutic action is attributed to the oxides, since their function is purely a cosmetic one. Mixtures of the two oxides can be made which simulate the color of the skin very closely.

2. *Calamine* (Calamina), U. S. P. XIII.—"Calamine is zinc oxide with a small amount of ferric oxide, and contains, after ignition, not less than 98 per cent of  $\text{ZnO}$ ." The presence of a small amount of iron oxide in calamine is not a deliberate thing. It is an inherent part of the mineral from which calamine is made, and while it does not impart any superior medicinal value to the zinc oxide with which it is associated, it does have the advantage of coloring the zinc oxide to more nearly simulate skin color than is true of pure zinc oxide (white). (See also p. 378.)

3. *Peptonized Iron* (Ferrum Peptonatum, Iron Peptone), N. F. VIII.—"Peptonized iron is a compound of iron oxide and peptone, rendered soluble by the presence of sodium citrate, and yields not less than 16 per cent and not more than 18 per cent of Fe." Average dose—0.3 Gm. (approximately 5 grains).

4. *Neocalamine Liniment* (Linimentum Neocalamineæ), N. F. VIII.—This preparation contains 150 Gm. of Prepared Neocalamine, 500 cc. of olive oil, and enough calcium hydroxide solution to make 1000 cc. The iron oxide is present in the form of Prepared Neocalamine (*q. v.*).

5. *Neocalamine Lotion* (*Lotio Neocalaminæ*), N. F. VIII.—This lotion contains 150 Gm. of Prepared Neocalamine, 400 cc. of bentonite (suspending agent), and enough water to make 1000 cc. of lotion. (See p. 378.)

6. *Phenolated Neocalamine Lotion* (*Lotio Neocalaminæ Phenolata, Compound Neocalamine Lotion*), N. F. VIII.—This preparation contains 1 per cent of liquefied phenol in Neocalamine Lotion. The phenol is added to provide some analgesic properties for relief of skin discomfort.

7. *Neocalamine Ointment* (*Unguentum Neocalaminæ*), N. F. VIII.—This ointment contains 15 per cent of Prepared Neocalamine in an ointment base composed of wool fat, petrolatum, liquid petrolatum and water.

8. *Prepared Neocalamine* (*Neocalamina Preparata*), N. F. VIII.—“Prepared Neocalamine is zinc oxide admixed with ferric oxide, and contains, after ignition, not less than 92 per cent of ZnO.” This preparation is made by mixing 30 Gm. of Red Ferric Oxide with 40 Gm. of Yellow Ferric Oxide and 930 Gm. of Zinc Oxide. It is a substitute for calamine and is superior in that the color has been made to simulate that of the skin more closely than is the case with calamine.

9. *N. F. Sun Cream* (*Cremor Solis N. F., Sun Tan Ointment*), N. F. VIII.—Red ferric oxide occurs in this preparation in the form of Neocalamine, although Yellow Ferric Oxide has been added in addition to what occurs in the Neocalamine. The purpose is, of course, to provide a better cosmetic preparation. This cream is used as a sun tan ointment and permits “tanning” without too much danger of sunburn.

### YELLOW FERRIC OXIDE

*Yellow Ferric Oxide*, N. F. VIII

Formula,  $\text{Fe}_2\text{O}_3$ . Molecular Weight, 159.70

**Physical Properties.**—This oxide occurs as a yellowish-orange powder, which closely approximates the color of Reference Yellow Ferric Oxide.<sup>1</sup> In its solubilities and particle size it is the same as the red ferric oxide.

**Chemical Properties.**—These are the same as those for red ferric oxide. However, the yellow variety contains more water of hydration than does the red form. This difference in water content is apparently responsible for the difference in color. The difference in water content is shown by the allowable loss on ignition for the two oxides. The red form is allowed only 3 per cent loss on ignition whereas the yellow form is allowed 12 per cent of its weight.

**Official Tests for Identity.**—The N. F. VIII does not set up standards for identification of this oxide, since the physical properties serve to identify it.

<sup>1</sup> Obtainable from Chairman of the Committee on National Formulary

**Commercial Manufacture.**—(See Red Ferric Oxide, p. 623.)

**Pharmaceutical Preparations and Uses.**—1. *Yellow Ferric Oxide* (*Ferri Oxidum Flavum*), N. F. VIII.—“Yellow Ferric Oxide contains not less than 97.5 per cent of  $\text{Fe}_2\text{O}_3$ , calculated on the basis of the ignited product, the loss on ignition being determined on a separate sample.” As previously noted, this oxide is used together with the red oxide for cosmetic purposes.

2. *Neocalamine Liniment* (*Linimentum Neocalaminæ*), N. F. VIII.—This liniment contains the Yellow Ferric Oxide occurring in the Prepared Neocalamine used in this liniment. (See p. 378.)

3. *Neocalamine Lotion* (*Lotio Neocalaminæ*), N. F. VIII.—This lotion contains Prepared Neocalamine, of which Yellow Ferric Oxide is an ingredient. (See p. 378.)

4. *Phenolated Neocalamine Lotion* (*Lotio Neocalaminæ Phenolata*, Compound Neocalamine Lotion), N. F. VIII.—This lotion contains the Yellow Ferric Oxide contained in Prepared Neocalamine used in this preparation. (See p. 379.)

5. *Neocalamine Ointment* (*Unguentum Neocalamineæ*), N. F. VIII.—This ointment contains the Yellow Ferric Oxide in the form of Prepared Neocalamine (see p. 379).

6. *Prepared Neocalamine* (*Neocalamina Præparata*), N. F. VIII.—This preparation contains Yellow Ferric Oxide, Red Ferric Oxide and zinc oxide. The iron oxides are for the purpose of giving a skin color to the preparation. Any therapeutic action is due to the 93 per cent of zinc oxide that is present. (See p. 378.)

7. *N. F. Sun Cream* (*Cremor Solis N. F.*, Sun Tan Ointment), N. F. VIII.—(See p. 624.)

## SOLUBLE FERRIC PHOSPHATE

*Soluble Ferric Phosphate*, N. F. VIII



**Physical Properties.**—This preparation occurs in the form of thin, bright green, transparent scales. It also occurs as granules. It is odorless and has an acidulous, slightly saline taste. Because it is discolored in the presence of moisture and light, it should be kept in well-closed containers protected from light.

This scale salt is freely soluble in water, but is insoluble in alcohol.

**Chemical Properties.**—Most of the iron in this preparation is bound in a non-ionized form. This is evidenced by the fact that it does not give a precipitate with ammonium hydroxide. It is, however, decomposed by alkali hydroxides to give a precipitate of ferric hydroxide.

**Official Tests for Identity.**—1. The addition of an excess of ammonia T.S. to aqueous solutions of this salt does not precipitate ferric hydroxide but does cause a reddish-brown color to form.

2. The iron is removed as ferric hydroxide from 10 cc. of an aqueous solution of the salt by boiling with sodium hydroxide T.S.

When the filtrate is strongly acidified, it responds to the magnesia mixture (*q. v.*) test for phosphate ion. If the precipitate of magnesium ammonium phosphate obtained in the phosphate test is treated with a few drops of silver nitrate T.S., it turns to a greenish-yellow color. This serves to distinguish it from pyrophosphate ion which does not give a color.

**Commercial Manufacture.**—This compound of undetermined composition is made by dissolving ferric citrate in distilled water with the aid of heat and then dissolving secondary sodium phosphate in the solution. The clear solution is evaporated to a thick syrup on a water-bath at a temperature not exceeding 60° C., and then spread on glass plates and dried. By scraping off the salt, it is obtained in the form of thin, bright green, transparent scales.

**Pharmaceutical Preparations and Uses.**—1. *Soluble Ferric Phosphate* (*Ferri Phosphas Solubilis, Ferric Phosphate with Sodium Citrate*), N. F. VIII.—“Soluble Ferric Phosphate is ferric phosphate rendered soluble by the presence of sodium citrate, and yields not less than 12 per cent and not more than 15 per cent of Fe.” This salt is very suitable for making liquid preparations of iron. It is non-irritating to the gastric system, and has a good hematinic action. Average dose—0.25 Gm. (approximately 4 grains).

2. *Iron, Quinine and Strychnine Phosphates Elixir* (*Elixir Ferri, Quininæ et Strychninæ Phosphatum, Elixir I. Q. S. Phosphates*), N. F. VIII.—This elixir contains 35 Gm. of Soluble Ferric Phosphate in 1000 cc. of the finished preparation. In addition, it contains quinine phosphate, strychnine phosphate, orange oil, alcohol, glycerin and distilled water. It is used as a bitter tonic with hematinic properties. Average dose—4 cc. (approximately 1 fluid-rachm).

### FERRIC SULFATE

Formula,  $\text{Fe}_2(\text{SO}_4)_3 \cdot 6\text{H}_2\text{O}$  (Approx.)

Molecular Weight, 399.86 (Anhydrous)

*Note: This salt is not official but because it exists in the form of its solution, it is included among the official compounds of iron.*

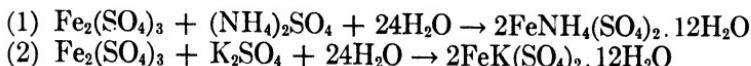
**Physical Properties.**—This salt is grayish-white in color, although the product of commerce which contains approximately 6 molecules of water of hydration is yellowish in color. It is very hygroscopic, and is slowly soluble in water. It is only sparingly soluble in alcohol.

**Chemical Properties.**—When dissolved in water this salt is acid in reaction due to hydrolysis. This property is common to other ferric salts.

Solutions of ferric sulfate give characteristic reactions of the ferric and sulfate ions.

In addition, ferric sulfate forms typical alums when treated with either ammonium sulfate (1) or potassium sulfate (2). These alums crystallize readily in bright, violet octahedra which effloresce in dry

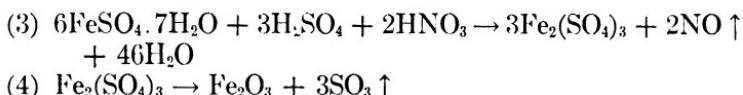
air. They are soluble in water but insoluble in alcohol. Because they contain ferric ions they act as styptics.



**Tests for Identity.**—Because ferric sulfate *per se* is not official, the tests for identity of Ferric Sulfate Solution will be given instead.

1. Ferric Sulfate Solution responds to the tests for *Ferric Ion* (*q. v.*) and also responds to the tests for *Sulfate Ion* (*q. v.*).

**Commercial Manufacture.**—Ferric sulfate can be obtained by adding nitric acid to a hot solution of ferrous sulfate containing sulfuric acid (3). The reaction mixture is then evaporated until the salt crystallizes or it may be standardized to contain the official requirement of iron and left in solution form. Care must be exercised in the evaporation of the material since it will decompose into ferric oxide and sulfur trioxide (4) if heated in a dry condition.



**Pharmaceutical Preparations and Uses.**—1. *Ferric Sulfate Solution* (Liquor Ferri Tersulfatis, Iron Tersulfate Solution), N. F. VIII.—“An aqueous solution containing  $\text{Fe}_2(\text{SO}_4)_3$ , corresponding to not less than 9.5 per cent and not more than 10.5 per cent of Fe.” This solution is a yellowish-brown, almost odorless liquid. It has an acid taste, and an acid reaction to litmus paper. It has a specific gravity of about 1.43 at 25° C. This preparation is not used internally, but is extensively employed in the preparation of the scale salts of iron. It has astringent and styptic properties.

## FERROUS CARBONATE

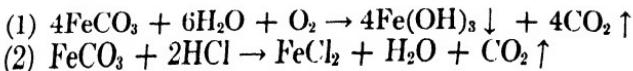
Formula,  $\text{FeCO}_3$ . Molecular Weight, 115.86

*Note:* *Ferrous carbonate is not official as such, but is official in the form of numerous preparations and, therefore, is discussed with the official salts of iron.*

**Physical Properties.**—Freshly precipitated ferrous carbonate is white in color. However, when in contact with air it quickly becomes green, and finally changes to brown. It is insoluble in water.

**Chemical Properties.**—Ferrous carbonate, as indicated, quickly changes from white to a green color and then to brown. These color changes are due to oxidative changes caused by atmospheric oxygen. Usually, the decomposition is attended by loss of  $\text{CO}_2$  and formation of ferric hydroxide (1). When treated with acids ferrous carbonate effervesces due to liberation of carbon dioxide (2), this reaction probably being the fate of ferrous carbonate when administered orally. On this basis, ferrous chloride has been advocated

as the most desirable form of ferrous salt to use since it eventuates in that form in the stomach.



Ferrous carbonate behaves in the same way that all carbonates do when treated with excess carbon dioxide, namely to form the soluble bicarbonate (3). Solutions of the bicarbonate are unstable in contact with air and quickly begin to deposit brown ferric hydroxide.

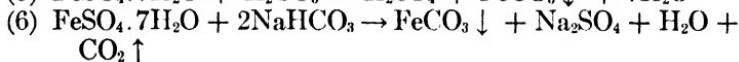
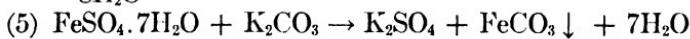
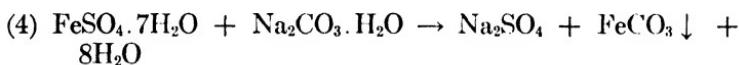


**Official Tests for Identity.**—No official tests for identity are available since the compound is not official as such. However, two tests are given in the monograph for *Saccharated Ferrous Carbonate*, N. F. VIII.

1. When 10 to 20 mg. of saccharated ferrous carbonate is treated with 5 cc. of hydrochloric acid, the material goes into solution with the copious evolution of carbon dioxide and the formation of a greenish-yellow liquid (2).

2. One Gm. of saccharated ferrous carbonate is dissolved in 5 cc. of hydrochloric acid and the resulting solution diluted to 100 cc. with distilled water. This solution gives tests for *Ferrous Salts* (*q. v.*).

**Commercial Manufacture.**—Ferrous carbonate occurs naturally as the mineral *siderite* ( $\text{FeCO}_3 \cdot \text{H}_2\text{O}$ ) or *spathic iron ore*. However, the commercial supplies for medicinal uses are made by adding sodium carbonate (4), potassium carbonate (5), or sodium bicarbonate (6) to solutions of ferrous sulfate.



Reaction (4) is used in the preparation of *Ferrous Carbonate Mass*, N. F. VIII. Reaction (5) is used in the preparation of *Ferrous Carbonate Pills*, N. F. VIII, and reaction (6) is used in the preparation of *Saccharated Ferrous Carbonate*, N. F. VIII. Reaction (6) is said to be an especially desirable way of making ferrous carbonate because it is attended with the formation of  $\text{CO}_2$  which helps to prevent oxidation of the ferrous carbonate which forms.

**Pharmaceutical Preparations and Uses.**—1. *Ferrous Carbonate Mass* (Massa Ferri Carbonatis, Vallet's Mass), N. F. VIII.—“Ferrous Carbonate Mass contains not less than 36 per cent and not more than 41 per cent of  $\text{FeCO}_3$ .” Ferrous sulfate and monohydrated sodium carbonate are each dissolved in specified amounts of water. To the iron solution is added syrup and, after cooling, the sodium

carbonate solution is added with stirring to that of the ferrous sulfate. The precipitated ferrous carbonate is allowed to subside, the supernatant liquid decanted and the precipitate then washed with a mixture of 1 volume of syrup to 19 volumes of distilled water (to prevent oxidation) until the washings no longer have a salty taste. The precipitate is then drained on a strainer, expressed and incorporated with sucrose and honey. The mixture is evaporated with constant stirring on a water-bath until it is reduced to the required weight. It is used effectively as a hematinic. Average dose—0.6 Gm. (approximately 10 grains).

2. *Ferrous Carbonate Pills* (Pilulae Ferri Carbonatis, Chalybeate Pills, Blaud's Pills, Ferruginous Pills), N. F. VIII.—“Each Pill contains not less than 60 mg. of  $\text{FeCO}_3$ .” Potassium carbonate is triturated in a mortar with a small amount of glycerin, and to this is added a mixture of ferrous sulfate and sucrose which previously have been intimately mixed. The mass is mixed thoroughly until it assumes a greenish color. When the reaction is complete, tragacanth and althea are added and enough distilled water to give a pilular consistency. The mass is then divided into the required number of pills. These pills are a favorite form of hematinic medication. To obtain best results it is desirable to have the pills freshly made. Average dose—5 pills.

3. *Saccharated Ferrous Carbonate* (Ferri Carbonas Saccharatus), N. F. VIII.—“Saccharated Ferrous Carbonate contains, in each 100 Gm., not less than 15 Gm. of  $\text{FeCO}_3$ .” A hot, slightly acidulated ( $\text{H}_2\text{SO}_4$ ) solution of ferrous sulfate and sucrose are added to a carefully prepared solution of sodium bicarbonate. In order to minimize hydrolysis, the solution of sodium bicarbonate should be effected at a temperature not above 50° C. The container is rotated to facilitate the chemical reaction. The precipitated ferrous carbonate is washed free from sodium sulfate with a hot mixture consisting of 1 volume of syrup and 19 volumes of distilled water, until the decanted liquid gives only a slight cloudiness with barium chloride T.S. The precipitate is drained, intimately mixed with sucrose and lactose, and evaporated to dryness on a water-bath. It is then reduced to a powder and sufficient well-dried sucrose added to make the required weight. This powder should be prepared in the shortest possible time in order to minimize the oxidation of ferrous carbonate.

In common with the other ferrous carbonate preparations, this is an effective hematinic. Average dose—0.25 Gm. (approximately 4 grains).

4. *Saccharated Ferrous Carbonate Capsules* (Capsulæ Ferri Carbonatis Saccharati), N. F. VIII.—“Saccharated Ferrous Carbonate Capsules contain  $\text{FeCO}_3$  equivalent to not less than 14.25 per cent and not more than 15.75 per cent of the labeled quantity of saccharated ferrous carbonate.” This is a convenient form of administering saccharated ferrous carbonate. Average dose—0.25 Gm. (approximately 4 grains) of Saccharated Ferrous Carbonate.

### FERROUS GLUCONATE

*Ferrous Gluconate*, N. F. VIII

Formula,  $\text{Fe}(\text{C}_6\text{H}_{11}\text{O}_7)_2 \cdot 2\text{H}_2\text{O}$ ;  $(\text{CH}_2\text{OH}(\text{CHOH})_4 \cdot \text{COO})_2\text{Fe} \cdot 2\text{H}_2\text{O}$

Molecular Weight, 482.18

**Physical Properties.**—This salt occurs as a fine, yellowish-gray or pale greenish-yellow powder. It has an odor suggesting burned sugar.

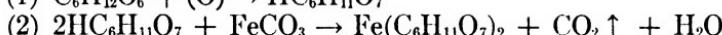
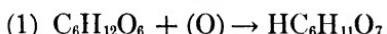
One Gm. is soluble in 4 cc. of water. It is nearly insoluble in alcohol.

**Chemical Properties.**—Its aqueous solutions are acid in reaction. The reactions of this salt in aqueous solution are essentially those of the ferrous salts (*q. v.*) and of the gluconate ion (*q. v.*).

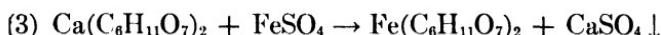
**Official Tests for Identity.**—1. Five cc. of a warmed 1 in 10 aqueous solution of the salt is treated with 0.65 cc. of glacial acetic acid and 1 cc. of freshly distilled phenylhydrazine and then warmed on a steam bath for thirty minutes. When allowed to cool it will deposit crystals of gluconic acid phenylhydrazide either spontaneously or with scratching of the test-tube walls. (For reactions see Calcium Gluconate, p. 324.)

2. A 1 in 20 solution responds to all tests for *Ferrous Salts* (*q. v.*).

**Commercial Manufacture.**<sup>1</sup>—To produce ferrous gluconate the first step is the production of gluconic acid by the fermentative oxidation of glucose (1). The solution of gluconic acid so obtained is then treated with ferrous carbonate to form soluble ferrous gluconate (2). From the resulting solution the ferrous gluconate is crystallized. The salt contains 2 molecules of water of crystallization. This is then dried and packaged.



It can also be made by the interaction of ferrous sulfate and calcium gluconate (3), although this method is not used commercially.



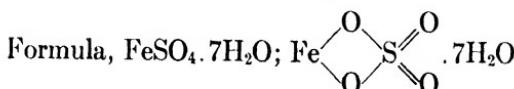
**Pharmaceutical Preparations and Uses.**—1. *Ferrous Gluconate* (Ferri Gluconas), N. F. VIII.—Ferrous Gluconate contains not less than 11.5 per cent of Fe, calculated on an anhydrous basis, the moisture being determined on a separate sample by drying at 105° for four hours. This preparation is one of the newer ferrous compounds to appear on the market. As previously pointed out, it has the advantage of causing much less gastric irritation than the other commonly used ferrous salts, *e. g.*, ferrous sulfate. It is obtainable commercially as tablets and elixir under the trade name "Fergon,"

<sup>1</sup> Private communication from Chas. Pfizer & Co., May 5 (1947).

and as capsules and elixir under its own name. Average dose—0.3 Gm. (approximately 5 grains).

### FERROUS SULFATE

*Ferrous Sulfate*, U. S. P. XIII



Molecular Weight, 278.02

**Physical Properties.**—The official salt occurs in the form of large pale bluish-green, monoclinic prisms having a density of 1.8987. It is odorless, and has a saline, styptic taste. In dry air the salt effloresces and becomes coated with a grayish-white powder of the anhydrous salt. In moist air the crystals rapidly oxidize to a brownish-yellow, basic ferric sulfate, which makes the salt unfit for use in medicinal preparations. When the crystals are slowly heated to  $115^\circ \text{ C}.$ , they disintegrate and lose most of their water of hydration.

Ferrous sulfate dissolves in 1.5 times its weight of water at  $25^\circ \text{ C}.$ , and in less than one-half its weight (0.5 cc.) of boiling water to form solutions that are acid to litmus paper.

**Chemical Properties.**—In general, it may be said that the reactions of ferrous sulfate are those of the ferrous ion and of the sulfate ion.

Ferrous sulfate combines with the alkali sulfates to form double salts. The most important one of these compounds is *ferrous ammonium sulfate*  $\text{FeSO}_4 \cdot (\text{NH}_4)_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ . This very stable salt is prepared by dissolving equimolecular weights of the two salts in water and crystallizing. It is known as Mohr's Salt and is used in analytical chemistry.

**Official Tests for Identity.**—This salt responds to the tests for *Ferrous Salts* (*q. v.*) and *Sulfate Ion* (*q. v.*).

**Commercial Manufacture.**—1. The best grade of ferrous sulfate is obtained by dissolving iron in diluted sulfuric acid and concentrating to crystallization.

2. The commercial grades of this salt are made by piling iron pyrites in heaps and exposing it to atmospheric oxidation (1). The mass is leached with water and the dilute solution of ferrous sulfate is run into large vats. Scrap iron is added to take care of any free sulfuric acid and to precipitate any copper ion present in the solution. The liquid is concentrated to crystallization.



3. Appreciable quantities of ferrous sulfate are obtained by concentrating the vat liquor obtained in the "pickling" of steel (*q. v.*).

**Pharmaceutical Preparations and Uses.**—1. *Ferrous Sulfate* (Ferri Sulfas, Iron Sulfate), U. S. P. XIII.—"Ferrous Sulfate contains not

less than 54.36 and not more than 57.07 per cent of anhydrous ferrous sulfate ( $\text{FeSO}_4$ ), corresponding to not less than 99.5 per cent of the hydrated salt ( $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ ).” This salt is the most popular of the ferrous salts as well as the most economical. It is an efficient hematinic. Average dose—0.3 Gm. (approximately 5 grains).

2. *Exsiccated Ferrous Sulfate* (Ferri Sulfas Exsiccatus, Dried Ferrous Sulfate), U. S. P. XIII.—“Exsiccated Ferrous Sulfate contains not less than 80 per cent of anhydrous ferrous sulfate ( $\text{FeSO}_4$ ).” Of the many forms in which ferrous sulfate exists, the exsiccated form is probably the most used, principally because it can be given in smaller doses than the form containing water of crystallization, and because it does not effloresce. It is made by allowing the hydrated salt to effloresce at a temperature of about 40° C. in dry air and then heating it with constant stirring on a water-bath until it is reduced to between 64 and 65 per cent of its original weight. The resulting material is reduced to a fine powder and immediately placed in dry, tightly stoppered bottles. Average dose—0.2 Gm. (approximately 3 grains).

3. *Ferrous Sulfate Tablets* (Tabellæ Ferri Sulfatis), U. S. P. XIII.—“Ferrous Sulfate Tablets contain not less than 95 per cent and not more than 110 per cent of the labeled amount of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ . An equivalent amount of exsiccated ferrous sulfate may be used in place of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ , in preparing the Tablets.” The tablets are merely a convenient form for administering ferrous sulfate. In general, the tablets containing the exsiccated form predominate, a typical example being “Feosol” tablets. A few firms market an enteric coated tablet which is supposed to eliminate the gastric discomfort occasionally encountered when ferrous sulfate is used. Despite claims that the enteric coated tablet cannot be absorbed very well since it is not exposed to the acid gastric juices but only to the alkaline intestinal juices, many physicians find that satisfactory hematinic responses are obtained. Average dose of Ferrous Sulfate—0.3 Gm. (approximately 5 grains).

4. *Ferric Subsulfate Solution* (Liquor Ferri Subsulfatis, Monsel’s Solution, Basic Ferric Sulfate Solution), N. F. VIII.—“Ferric Subsulfate Solution is an aqueous solution containing, in each 100 cc., basic ferric sulfate equivalent to not less than 20 Gm. and not more than 22 Gm. of Fe.” Coarsely powdered ferrous sulfate is added in four approximately equal portions to a mixture of sulfuric and nitric acids which has previously been heated to nearly 100° C. Nitric acid is added, drop by drop, to the constantly stirred hot solution until red fumes cease to be evolved and the liquid has assumed a dark, reddish brown color. The solution is boiled until free from nitric acid, maintaining the volume at about 1000 cc. by the addition of distilled water as needed and, when cool, diluted with distilled water to the required volume. The product is filtered; if necessary, until clear.

Ferric Subsulfate Solution is a dark, reddish-brown liquid,

odorless or nearly so, with a sour, strongly astringent taste. At 25° C. it has a specific gravity of about 1.548, and is miscible with both water and alcohol.

Solution of subsulfate of iron will sometimes congeal to a semi-solid mass when cooled or upon long standing. The application of gentle heat will restore it to the liquid state.

Ferric subsulfate is of variable composition and therefore the reaction cannot be definitely expressed in the form of an equation. The following equation has been suggested as being representative (2).



When concentrated sulfuric acid is gradually added to a solution of subsulfate of iron, the color becomes lighter, and white anhydrous ferric sulfate is precipitated when the quantity of acid reaches one-half the volume of the iron solution. Ferric Sulfate Solution, however, does not give a precipitate of anhydrous ferric sulfate when treated with concentrated sulfuric acid. As a styptic—use it undiluted.

5. *Ferrous Carbonate Mass* (Massa Ferri Carbonatis, Vallet's Mass), N. F. VIII.—(See p. 628.)

6. *Ferrous Carbonate Pills* (Pilulæ Ferri Carbonatis, Chalybeate Pills, Blaud's Pills, Ferruginous Pills), N. F. VIII.—(See p. 629.)

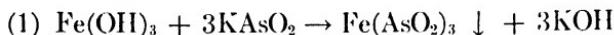
7. *Saccharated Ferrous Carbonate* (Ferri Carbonas Saccharatus), N. F. VIII.—(See p. 629.)

8. *Ferrous Sulfate Syrup* (Syrupus Ferri Sulfatis), N. F. VIII.—“Ferrous Sulfate Syrup contains, in each 100 cc., not less than 3.75 Gm. and not more than 4.25 Gm. of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ .” It is prepared by dissolving ferrous sulfate (40 Gm.), citric acid (2.1 Gm.), peppermint spirit (2 cc.) and 200 Gm. of sucrose in 450 cc. of distilled water, and filtering until the solution becomes clear. Then 625 Gm. of sucrose are dissolved in the clear filtrate and the volume brought to 1000 cc. with distilled water. This form of ferrous sulfate is convenient for administration, especially for children. It also possesses a flexibility of dosage not possible with the tablets. Average dose—8 cc. (approximately 2 fluidrachms).

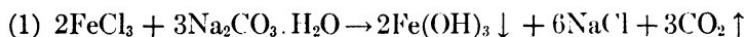
#### NON-OFFICIAL COMPOUNDS OF IRON

**Ferric Hydroxide**  $[\text{Fe}(\text{OH})_3]$ .—Ferric hydroxide is formed as a brown gelatinous precipitate when an alkali hydroxide is added to a solution of a ferric salt. The precipitate is insoluble in an excess of the precipitant but readily dissolves in hydrochloric acid. When the freshly precipitated ferric hydroxide is boiled in or allowed to stand in contact with water, it is gradually converted first into the basic hydroxide  $[\text{Fe}_2\text{O}(\text{OH})_4$  or  $\text{Fe}_2\text{O}_3 \cdot 2\text{H}_2\text{O}$ ] and then into a bright red, amorphous powder having the composition  $\text{Fe}_2\text{O}_2(\text{OH})_2$  or  $\text{Fe}_2\text{O}_3 \cdot \text{H}_2\text{O}$ . Ferric hydroxide strongly tends toward forming colloidal solutions. Thomas Graham obtained a colloidal solution

by dissolving freshly precipitated ferric hydroxide in a solution of ferric chloride and then dialyzing the solution. Such solutions are known as "dialyzed iron," and are said to contain about 98.5 per cent of colloidal ferric hydroxide and about 1.5 per cent of ferric chloride. Ferric hydroxide is very feebly basic and dissolves in very strong bases to form ferrites. Freshly precipitated ferric hydroxide reacts very quickly with soluble arsenic compounds to form insoluble ferric salts (1). Therefore, it was at one time known as the Official Arsenic Antidote. It is held in less esteem in present-day medicine because it is only effective if used as a gastric lavage immediately following arsenic poisoning. If used, it should be freshly made because it loses its activity upon standing.



**Ferri Oxidum Saccharatum** (Saccharated Ferric Oxide, Soluble Ferric Oxide, Ferrum Oxydatum Saccharatum, Eisenzucker), N. F. VII, contains, in each 100 Gm., the equivalent of not less than 2.8 Gm. and not more than 3.2 Gm. of Fe. This preparation consists of a mixture of sugar and ferric saccharate,  $\text{C}_{12}\text{H}_{22}\text{O}_{11}(\text{Fe}_2\text{O}_3)_2 + \text{C}_{12}\text{H}_{22}\text{O}_{11}\text{Na}_2\text{O}$ . It is prepared by adding a solution of ferric chloride to a solution of monohydrated sodium carbonate (1).



The liquid is decanted and the ferric hydroxide washed with distilled water until a portion of the washings, when diluted with 5 volumes of distilled water, gives only a slight opalescence with  $\text{AgNO}_3$  T.S. The precipitate is transferred to a porcelain dish, sugar and a sufficient quantity of a 15 per cent solution of sodium hydroxide to produce a clear solution, is added. The mixture is then evaporated to dryness on a water-bath. Average dose—Metric, 2 Gm.; Apothecaries, 30 grains.

**Ferric Pyrophosphate**  $[\text{Fe}_4(\text{P}_2\text{O}_7)_3 \cdot 9\text{H}_2\text{O}]$ .—This salt is formed as a yellowish-white precipitate when a solution of sodium pyrophosphate is treated with ferric sulfate. Although insoluble in water, it readily dissolves in solutions of the alkali citrates to form green solutions.

Ferric pyrophosphate was recognized under the title, *Ferri Pyrophosphas Solubilis* in the seventh edition of the *National Formulary*. It was described as "ferric pyrophosphate rendered soluble by the presence of sodium citrate, and yields not less than 10.5 per cent and not more than 12.5 per cent of Fe." This compound is made by dissolving unefloresced sodium pyrophosphate in an aqueous solution of ferric citrate. The solution is concentrated to a syrupy consistency on a water-bath at a temperature not exceeding 60° C. and then spread on glass plates and dried. When scraped from the plates, the salt occurs in thin, transparent, odorless, apple-green scales. It also occurs in pearls or granules. The "scale salt" is readily soluble with a slightly acid reaction in water. It is insoluble

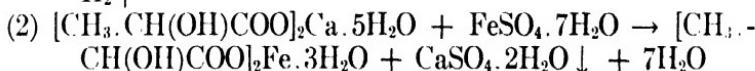
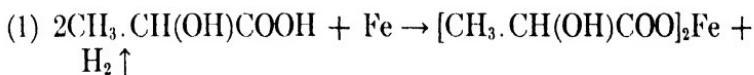
in alcohol. Moist air and light decompose it. Average dose—Metric, 0.25 Gm.; Apothecaries, 4 grains.

**Ferrous Chloride** ( $\text{FeCl}_2$ ).—Native ferrous chloride is known as *Lawrencite*. White, shining crystals of anhydrous ferrous chloride may be obtained by passing hydrogen chloride over red hot iron or by reducing ferric chloride in a current of hydrogen. Greenish-blue, monoclinic crystals of the tetrahydrate ( $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ ) are obtained by evaporating *in vacuo* a solution of iron or iron carbonate in hydrochloric acid. The salt is very unstable as it deliquesces in air and effloresces in a desiccator. It is readily soluble in water and in alcohol. When heated in air, it decomposes into ferric oxide and ferric chloride but when heated in steam it forms the ferroso-ferric oxide, hydrochloric acid, and hydrogen. It unites directly with ammonia to form an addition product,  $\text{FeCl}_2 \cdot 3\text{NH}_3$ , which loses ammonia when heated.

Ferrous chloride is used medicinally in the form of an elixir for its hematinic properties. (See also p. 627.)

**Ferrous Lactate** [ $\text{Fe}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 3\text{H}_2\text{O}$ ] (N. N. R., 1947).—It occurs as a greenish-white crystalline powder, or in crystalline crusts. It is slowly soluble in about 40 parts of water at  $25^\circ \text{ C}.$ , and in 12 parts of boiling water, giving solutions that are slightly acid to litmus. Alkali citrates form green solutions of the salt. It is nearly insoluble in alcohol.

It can be made by digesting iron with lactic acid (1). When the reaction has ceased, the solution is filtered, concentrated, and crystallized. It may be obtained also by dissolving crystallized calcium lactate in water and then agitating the solution with ferrous sulfate (2). Alcohol is then added to facilitate the separation of calcium sulfate, the mixture is filtered, and the filtrate evaporated to crystallization.



Ferrous lactate is sometimes employed in the treatment of chlorosis. It is said that very little, if any, gastric irritation follows the administration of ferrous lactate. Average dose—Metric, 0.3 Gm.; Apothecaries, 5 grains.

## CHAPTER XLV

### COBALT AND COBALT COMPOUNDS

#### COBALT

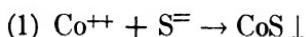
Symbol, Co. Valence, II, III. Atomic Weight, 58.94;  
Atomic Number, 27

**History and Occurrence.**—At one time, the name "cobalt" was given to a certain mineral which was used to produce a blue color in glass. In 1735, G. Brandt succeeded in preparing an impure cobalt which he called *Kobalt-rex*. It is said that the element obtained its name from the German word *der Kobold* ("a goblin or gnome"). This name was used to designate iron ores from which it was thought to be impossible to obtain metallic iron because of the interference of evil spirits.

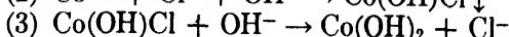
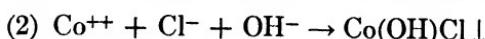
This metallic element is usually found in Nature associated with nickel, iron, copper, and silver minerals in the form of arsenides and sulfarsenides [*smaltite*, CoAs<sub>2</sub>, *speiss-cobalt* (Co, Ni, Fe)As<sub>2</sub>, *cobalt glance* (CoFeAs)S<sub>2</sub>, *cobaltite*, CoAsS]. It occurs also as the sulfides (*linnæite*, Co<sub>3</sub>S<sub>4</sub>, *syepoorite*, CoS), arsenate (*erythrite* [cobalt bloom], Co<sub>3</sub>As<sub>2</sub>O<sub>7</sub>.8H<sub>2</sub>O), and as mixed oxides of cobalt and manganese (*asbolite*, *wad*, CoMnO<sub>2</sub>.2MnO<sub>2</sub>.4H<sub>2</sub>O). Nearly all of the cobalt used in the United States is imported from Europe, where most of it is recovered as a by-product from the smelting of copper ores obtained from Belgian Congo. The silver ore deposits near Cobalt, Ontario, are rich in cobalt, and now supply the United States with large quantities. It is estimated that the World production of cobalt in 1946 was 597 metric tons.

**Properties.**—Pure cobalt is a pinkish-white metal having a specific gravity of 8.8 at 20° C. It is harder than iron, possesses magnetic properties, and melts at 1480° C. It boils at 2900° C. It crystallizes in the cubic system.

**Chemical Properties.**—It dissolves slowly in dilute acids and, like iron, exhibits the phenomenon of passivity (*q. v.*). Cobalt forms two series of salts, *cobaltous* and *cobaltic*. Cobalt reacts with carbon monoxide to form carbonyls. The following equations represent some of the reactions of cobalt in solution. 1. Alkali sulfides precipitate black, cobaltous sulfide from solutions of cobaltous salts (1).



2. Fixed alkali hydroxides precipitate blue basic salts, which rapidly change to an olive green color (2). If boiled soon after its precipitation, the color changes from blue to pink, due to the formation of cobaltous hydroxide [Co(OH)<sub>2</sub>] (3).



3. Ammonium hydroxide precipitates blue basic salts from solutions of cobaltous salts. The precipitates are soluble in an excess of the reagent and form bright colored solutions of complex ammonio-cobaltous hydroxide  $[Co(NH_3)_6(OH)_2]$  which rapidly oxidize to ammonio-cobaltic hydroxide  $[Co(NH_3)_6(OH)_3]$ .

4. Alkali carbonates precipitate reddish, basic cobaltous carbonate  $[Co_8O_5(CO_3)_3]$ , which turns violet to blue when boiled.

5. When a solution of a cobaltous compound is warmed with potassium chloride, potassium nitrite, and acetic acid, a yellow precipitate of potassium cobaltinitrite is formed (4).



6. When cobalt compounds are fused into a borax bead, a blue color (due to cobalt metaborate,  $Co(BO_2)_2$ ) is produced.

7. When a fused aluminum compound is moistened with a solution of cobalt nitrate, a blue color (due to cobalt aluminate,  $Co[AlO_2]_2$ ) is produced.

8. Vogel's reaction: When a concentrated solution of ammonium thiocyanate is added to a cobaltous solution, ammonium cobalto-thiocyanate (beautiful blue) is formed (5). Ferric ion interferes with this test but may be removed by the addition of stannous chloride.



**Commercial Manufacture.**—Cobalt can be obtained (1) by the reduction of the monoxide or chloride with hydrogen or carbon monoxide, (2) by the Goldschmidt process, (3) by heating the oxalate under a layer of powdered glass, (4) by the electrolysis of the chloride, and (5) by chemical solution and precipitation.

**Pharmacological Action of the Cobalt Ion.**—Cobalt salts administered by parenteral injection cause marked circulatory effects such as a fall in blood pressure and general capillary damage. The blood pressure is lowered, probably by injuring the blood vessels. There are convulsive movements which indicate central nervous system stimulation followed by tremors and chorea-like movements, later by tetanus, and finally paralysis.

When taken orally cobalt salts may induce vomiting and diarrhea. They are not especially irritating to mucous membrane. The salts are rapidly absorbed from the intestinal tract and are excreted largely in the urine. Nephritis may result from kidney damage.

**Uses.**—The principal use of cobalt metal is in the manufacture of special steels (*q. v.*) and alloys. Cobalt alloys are very hard, resist oxidation, take a high polish, and maintain their temper even at high temperatures.

Cobalt has been found to stimulate the hematopoietic system when ingested in extremely small quantities over a period of time. This element is essential in the development of erythrocytes and hemoglobin. It is believed to stimulate the bone marrow. As far

as is known cobalt does not effect leukocyte formation. Since only traces of cobalt are necessary for the body and this amount is in the daily diet, there is little occasion to administer it.

### COBALT COMPOUNDS

**Oxides and Hydroxides.**—**Cobaltous Oxide** ( $\text{CoO}$ ).—This gray to greenish oxide is obtained (1) by heating the blue cobaltous hydroxide ( $\text{Co}[\text{OH}]_2$ ) or carbonate ( $\text{CoCO}_3$ ) in air, (2) by carefully heating cobalt oxalate ( $\text{CoC}_2\text{O}_4$ ) in a current of hydrogen or (3) by heating the cobalto-cobaltic oxide ( $\text{Co}_3\text{O}_4$ ) in a current of carbon dioxide. It has a density of 5.68 and decomposes at about  $800^\circ \text{ C}$ . It dissolves easily in warm, dilute mineral acids forming cobaltous salts. When a mixture of pure sand, potassium nitrate and cobaltous oxide is fused and the cooled product ground and powdered, the product is known as *smaut*. This blue powder contains from 6 to 16 per cent of cobalt and is used as a paint pigment and also in the ceramic industries. When cobaltous oxide is fused with zinc oxide, a green mass results. When the material is powdered, it is known as *Rinman's Green*. It is used also as a paint pigment. Cobaltous oxide is used in the manufacture of cobalt glass (blue glass).

**Cobaltous Hydroxide** [ $\text{Co}(\text{OH})_2$ ].—(See Chemical Properties.)

**Cobaltic Oxide** ( $\text{Co}_2\text{O}_3$ ).—This oxide is obtained as a velvety black powder by heating the nitrate or cobaltic hydroxide just sufficiently to effect decomposition (about  $180^\circ \text{ C}$ .) but not enough to form the  $\text{Co}_3\text{O}_4$ .

**Cobaltic Hydroxide** [ $\text{Co}(\text{OH})_3$ ].—Cobaltic hydroxide is made by adding a solution of an alkali hypochlorite to a solution of a cobalt salt, or by passing chlorine through an aqueous suspension of cobaltous hydroxide or carbonate. This hydroxide dissolves in cooled acids to form solutions of rather unstable cobaltic salts.

**Cobalto-cobaltic Oxide** ( $\text{Co}_3\text{O}_4$ ) is the most stable oxide of cobalt. It is made by heating any of the oxides or hydroxides, the carbonate, nitrate, or oxalate to a dull red heat in air or oxygen. It has been used externally as an astringent antiseptic powder.

**Halogen Salts.**—**Cobaltous Chloride** ( $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ ).—Cherry-red, prismatic crystals of this salt are obtained by crystallizing the salt from a solution made by the action of hydrochloric acid on cobaltous oxide. The anhydrous salt is blue in color and may be made by heating the crystalline hexahydrate; by burning the metal in chlorine; or by heating the sulfide in a current of chlorine. Cobaltous chloride has been used for many years as the basis for *invisible* or *sympathetic inks*. When a dilute solution of cobaltous chloride is used as a writing fluid, the marks are almost indiscernible. However, when the paper is warmed, the deposited salt is dehydrated and turns blue, thus making the marks distinctly visible. The blue color soon fades again in contact with air containing moisture. Cobaltous chloride combines directly with ammonia

to form a long series of complex derivatives, *e. g.*,  $\text{CoCl}_2 \cdot \text{NH}_3$ ,  $\text{CoCl}_2 \cdot 2\text{NH}_3$  (alpha and beta),  $\text{CoCl}_2 \cdot 4\text{NH}_3$ ,  $\text{CoCl}_2 \cdot 5\text{NH}_3$ . It is used in the manufacture of barometers, hydrometers, etc. It is used in military and industrial gas masks that are especially designed for protection against ammonia gas.

**Cobaltous Bromide** ( $\text{CoBr}_2 \cdot 6\text{H}_2\text{O}$ ).—Cobaltous bromide (pale red to violet crystals) closely resembles the chloride and may be prepared in a similar manner. It is used in the manufacture of hygrometers.

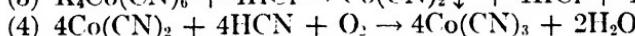
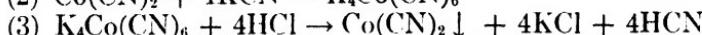
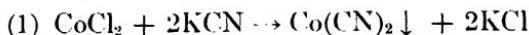
**Cobaltous Iodide** ( $\text{CoI}_2 \cdot 6\text{H}_2\text{O}$ ).—Cobaltous iodide is obtained as a grayish-green mass by heating cobalt and iodine together. It dissolves in water to give a red solution from which red hexagonal prisms of the hexahydrate ( $\text{CoI}_2 \cdot 6\text{H}_2\text{O}$ ) may be crystallized. These effloresce easily at  $27^\circ\text{C}$ . It is used in making hygrometers.

**Cobaltous Nitrate** [ $\text{Co}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ ].—Red, deliquescent, monoclinic prisms of this hexahydrate are obtained when a solution of the metal, its hydroxide, or carbonate in nitric acid is evaporated. It is readily soluble in water and in alcohol. It is used in making cobalt pigments and in invisible inks. The nitrate forms an insoluble compound with cyanides ( $\text{CN}^-$ ) and has been suggested as an antidote in cases of poisoning. Because of the speed of cyanide poisoning no antidote is very successful.

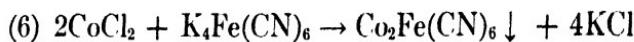
**Cobaltous Sulfate** ( $\text{CoSO}_4 \cdot 7\text{H}_2\text{O}$ ).—Dark red, monoclinic prisms of this salt are deposited when a solution of cobalt, cobalt oxide, or cobalt carbonate in dilute sulfuric acid is concentrated. The crystals are isomorphous with ferrous sulfate. The anhydrous salt is obtained by warming a solution of these crystals in concentrated sulfuric acid.

**Cobaltous Sulfide** ( $\text{CoS}$ ).—This compound can be obtained in bronze colored crystals by heating cobaltous oxide with sulfur, or by fusing a mixture of anhydrous cobaltous sulfate, barium sulfide and sodium chloride. It is obtained as a black, hydrated precipitate by the action of alkali sulfides upon cobaltous salts. In the moist state it readily oxidizes into forms that are less easily soluble in acids than the freshly precipitated sulfide.

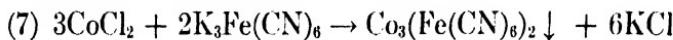
**Simple and Complex Cobalt Cyanides.**—Alkali cyanides, *e. g.*,  $\text{KCN}$ , precipitate a brownish-white, cobaltous cyanide from solutions of cobaltous salts (1). This precipitate dissolves in an excess of the precipitants to form colorless, double cyanides (2). Cold dilute acids reprecipitate cobaltous cyanide (3). When a solution of an alkali cobaltocyanide is digested with a few drops of hydrochloric acid ( $\text{KCN} + \text{HCl} \rightarrow \text{KCl} + \text{HCN}$ ), the alkali cobaltcyanide is produced (distinction from nickel) (4 and 5).



Potassium ferrocyanide precipitates grayish-green *cobaltous ferrocyanide* from solutions of cobaltous salts (6).



Potassium ferricyanide precipitates brownish-red cobaltous ferricyanide from solutions of cobaltous salts (7).



In the presence of ammonium chloride and ammonium hydroxide, potassium ferricyanide produces a blood-red color in solutions of cobaltous salts (distinction from nickel).

## CHAPTER XLVI

### NICKEL AND NICKEL COMPOUNDS

#### **NICKEL**

Symbol, Ni. Valence, II or III. Atomic Weight, 58.69;  
Atomic Number, 28

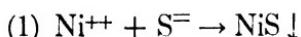
**History and Occurrence.**—This metallic element has been known from earliest times. Many centuries before Christ, the Chinese smelted ores containing nickel and copper with those of zinc and tin to make an alloy called *paksong*. This they used in making coins, ornaments, etc. An ore composed of nickel arsenide (NiAs) was known in 1694. This natural product closely resembled ores rich in copper. However, when it failed to yield any copper upon smelting, it was called "Old Nick's copper" or *Kupfernickel*, the word from which this element gets its name. In 1751, A. F. Cronstedt obtained the metal in an impure state from *niccolite* and the results of his work were corroborated in 1775 by T. O. Bergman.

Nickel occurs free and also alloyed with iron in meteorites. The principal ore deposits are around Sudbury, Ontario, and in the French Colony of New Caledonia in the South Pacific. The ores of the Sudbury district consist of copper-nickel-iron sulfides (*pyrrhotite*, *chalcopyrite* and *pentlandite*) associated with more or less cobalt, whereas, those of New Caledonia, known as *garnierite* from their discoverer, J. Garnier (1865), are hydrated silicates of nickel and magnesium, approximating the formula  $H_2(Ni, Mg)SiO_4 \cdot (H_2O)_n$ .

**Physical Properties.**—Nickel is a lustrous, white metal having a density of 8.9. Sometimes it has a slightly grayish or yellowish tinge. It is malleable and ductile, takes a high polish, is very hard, and possesses magnetic properties when exposed to moist air. It melts at  $1452^{\circ} C.$  and boils at  $2900^{\circ} C.$

**Chemical Properties.**—The metal slowly becomes covered with a superficial film of oxide. Dilute acids slowly act upon nickel and liberate hydrogen. It is readily attacked by dilute nitric acid. The metal resists the corrosive action of alkalies.

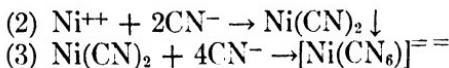
Solutions of nickel salts respond to the following chemical reactions: 1. Alkali sulfides precipitate black nickel sulfide from solutions of nickel salts (1).



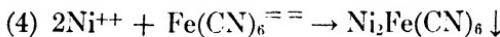
2. From solutions of nickel salts, fixed alkali hydroxides precipitate pale-green nickel hydroxide  $[Ni(OH)_2]$  which is insoluble in excess of alkalies, but dissolves in ammonium hydroxide or ammonium salts to form blue solutions containing the complex,  $Ni(NH_3)_6 \cdot (OH)_2$ .

3. Alkali carbonates precipitate a green, basic nickelous carbonate of variable composition  $[Ni_5(OH)_6(CO_3)_2]$ . The precipitate dissolves in ammonium hydroxide or ammonium salts to form blue solutions.

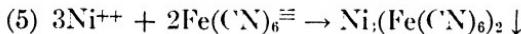
4. Potassium cyanide precipitates yellowish-green nickel cyanide from solutions of nickel salts (2). The precipitate dissolves in an excess of the precipitant to form double cyanides (3).



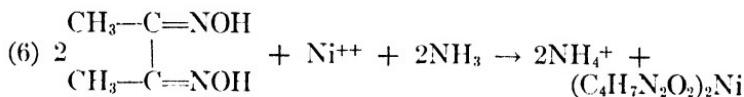
5. Potassium ferrocyanide precipitates greenish-white nickel ferrocyanide from solutions of nickel salts (4).



Potassium ferricyanide precipitates greenish-yellow nickel ferricyanide from solutions of nickel salts (5).



6. If dimethylglyoxime is added to an ammoniacal solution of a nickel salt, a bright red, insoluble, crystalline precipitate is obtained. Cobalt does not react with this reagent.



7. Nickel colors the borax bead brown in the oxidizing flame. The color is masked by a small amount of cobalt. In the reducing flame, metallic nickel "clouds" the bead.

**Commercial Manufacture.**—The ore containing sulfides of copper, nickel, and iron (*pentlandite*) is roasted to convert the sulfur and iron to oxides and then smelted in a blast furnace. This blasting usually removes all but a very small amount (less than 1 per cent) of iron and a *matte* is obtained which consists of about 40 per cent of copper-nickel alloy and 60 per cent of sulfur. The larger part of the sulfur is burned off in a Bessemer converter and a product containing about 80 per cent of the copper-nickel alloy is obtained. This alloy (*Monel metal*) is more resistant to corrosion than steel and is used for wire, screens, sheet-metal, etc.

Pure nickel may be made from this copper-nickel alloy either by the Browne electrolytic process or by the Mond process.

In the Browne electrolytic process, the bessemerized matte is crushed, roasted and reduced in a reverberatory furnace to metal, which is cast into anode plates. When these are electrolyzed, the nickel goes into solution, any copper remaining therein is precipitated as sulfide and the iron is removed as hydroxide with caustic soda. The solution is then concentrated, the precipitated sodium chloride filtered off, and the hot solution of nickel chloride again electrolyzed.

In the Mond process, the copper-nickel matte is crushed, treated with warm, dilute sulfuric acid to remove the copper and the residue reduced with cold water gas in a tower to a yellow, volatile nickel tetracarbonyl ( $\text{Ni}[\text{CO}]_4$ ). This liquid carbonyl boils at  $43^\circ\text{ C}$ ., and decomposes at  $200^\circ\text{ C}$ . into pure nickel and carbon monoxide. It will be noted that cobalt does not form a carbonyl under the above conditions.

**Pharmacological Action of Nickel Ion.**—(See Pharmacology of Cobalt Ion, p. 637.) The actions of Ni and Co are almost identical.

**Uses.**—Nickel is used extensively in the form of its alloys for making domestic utensils, coins, surgical instruments, automobile parts, chemical apparatus, etc. A nickel, zinc and copper alloy forms the well-known German silver. Finely divided nickel is a very active catalyst and is extensively used in the hydrogenation of cottonseed and linseed oils and other unsaturated organic compounds.

#### NICKEL COMPOUNDS

**Oxides and Hydroxides.**—**Nickel Monoxide** ( $\text{NiO}$ ).—This oxide occurs in Nature as the mineral *bunsenite*. It can be prepared by heating nickel hydroxide, carbonate, or nitrate. It is a green, crystalline powder which turns yellow on heating. It is used in the preparation of the nickel salts and in porcelain painting.

**Nickelous Hydroxide** [ $\text{Ni}(\text{OH})_2$ ].—Nickelous hydroxide is obtained as an apple-green, flocculent precipitate when an alkali hydroxide is added to a solution of a nickel salt. (See p. 641.) It is used in the production of nickel salts.

**Nickelic Oxide** ( $\text{Ni}_2\text{O}_3$ ) (*Nickel Peroxide, Sesquioxide*).—This oxide is obtained as a black powder by gently heating the carbonate or nitrate in air. It dissolves in oxyacids, such as nitric and sulfuric acids, with the evolution of oxygen and in hydrochloric acid with the liberation of chlorine. When strongly heated with oxygen, it is converted into  $\text{Ni}_3\text{O}_4$ . It is used in the production of oxygen and in storage batteries.

**Nickelic Hydroxide** [ $\text{Ni}(\text{OH})_3$ ].—Nickelic hydroxide is prepared as a black powder by adding a hypochlorite (or other strong oxidizing agent) to a solution of a nickel salt, or by passing chlorine through an aqueous suspension of nickelous hydroxide.

**Nickelous Chloride** ( $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ ).—Nickelous chloride is obtained in green, monoclinic prisms when a solution of nickel oxide in hydrochloric acid is concentrated and allowed to crystallize. When heated to  $140^\circ\text{ C}$ ., the salt loses water and is converted into the yellow anhydrous form. It is used in nickel-plating cast zinc, in the manufacture of sympathetic ink, etc. When the anhydrous salt is exposed to the action of ammonia or ammonium salts, it forms additive ammonia and ammonium compounds, *e. g.*,  $\text{NiCl}_2 \cdot 6\text{NH}_3$ ,  $\text{NH}_4\text{Cl} \cdot \text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ . This property has led to its use in military and industrial ammonia-gas masks.

**Nickelous Sulfate** ( $\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$ ).—When nickel oxide is dissolved in a slight excess of sulfuric acid and the resulting solution evaporated, bluish-green, quadratic pyramids of the hexahydrate crystallize out. If the crystallization is carried on at a temperature between 50° and 70° C., green, monoclinic crystals having the same amount of water of hydration are deposited. The salt crystallizes from nearly neutral solutions in green rhombic crystals containing 7 molecules of water. This salt is used as a mordant in dyeing and in printing textiles. A 1 or 2 per cent solution of nickel sulfate is sometimes employed as a parasiticide in certain skin diseases. It is used also for blackening zinc and brass.

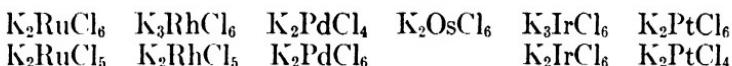
When an acidified (sulfuric acid) aqueous solution of nickel sulfate is mixed with a solution of ammonium sulfate and the solution concentrated, green crystals of the double sulfate [ $\text{NiSO}_4 \cdot (\text{NH}_4)_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ ] separate out. An ammoniacal solution of this double salt is used as the electrolyte for electroplating.

**Nickel Sulfide** ( $\text{NiS}$ ).—Nickel sulfide occurs in Nature as *millerite*. When obtained by heating nickel with sulfur or by subjecting nickel monoxide at red heat to the action of hydrogen sulfide, the product is a stable, yellow, somewhat crystalline mass. However, when prepared by adding ammonium sulfide to a solution of a nickel salt, it is thrown down as a black precipitate (nickel-equation 1). Nickel sulfide prepared in this way is said to exist in three modifications, which differ from one another by their solubilities in mineral acids.

## CHAPTER XLVII

### THE PLATINUM METALS AND THEIR COMPOUNDS

**Introduction.**—*Ruthenium* (Ru; atomic weight, 101.7), *rhodium* (atomic weight, 102.91), *palladium* (Pd; atomic weight, 106.7), *osmium* (Os; atomic weight, 190.2), *iridium* (Ir; atomic weight, 193.1) and *platinum* (Pt; atomic weight, 195.23) are collectively known as the “platinum metals” because they occur together in alluvial sands and gravels and because they resemble the most important member of the group, *platinum*. Ruthenium, rhodium and palladium have atomic numbers of 44, 45 and 46, respectively, and form the second set of triads of Group VIII. These metals are closely related to each other and are often called the “light metals of the platinum group” because their densities are approximately one-half those of the metals forming the third set of triads, *viz.*, osmium, iridium and platinum. Their melting-points are very high, and range from about 1700° to 2500° C. The platinum metals are polyvalent, the valences ranging from 1 to 8. They are chemically inactive. They are not affected by air or oxygen at ordinary temperatures. Osmium and ruthenium burn when finely divided and strongly heated. Sodium formate reduces their metallic salts to the free metals. Possibly their most notable similarity is the formation of halogen and cyanogen derivatives, *e. g.*



The salts of the oxygen acids of these metals are not very stable.

Aqua regia dissolves ruthenium, palladium, osmium, and platinum, whereas rhodium and iridium are only slightly attacked by it. Nitric acid acts upon palladium to form the nitrate  $[\text{Pd}(\text{NO}_3)_2]$ , and upon finely divided osmium to form  $\text{OsO}_4$ .

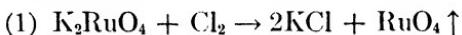
Very small quantities of these elements seem to be quite widely distributed in Nature. A large percentage (nearly 90 per cent) of the world's supply of these metals comes from the Urals and the Caucasus, Columbia, California, Australia, Canada, and Borneo supply the rest. According to reports, extensive deposits have been discovered recently in Africa.

#### RUTHENIUM

Symbol, Ru. Valence, II, III, IV, VI, VII, and VIII  
Atomic Weight, 101.7; Atomic Number, 44

Ruthenium was discovered by Claus in 1845. This element is a dark gray or black metal. It is very hard and brittle. It has a density of 12.26 and melts at about 2450° C. When finely divided

and heated to 600° C., the dioxide ( $\text{RuO}_2$ ) is formed. When sublimed, it forms green iridescent crystals. Its other oxides are  $\text{Ru}_2\text{O}_3$  and  $\text{RuO}_4$  (yellow volatile peroxide). Ruthenium forms several chlorides, *e. g.*,  $\text{RuCl}_2$ ,  $\text{RuCl}_3$  and  $\text{RuCl}_4$ . The addition of an alkali hydroxide to a solution of  $\text{RuCl}_3$  produces the hydroxide  $\text{Ru}(\text{OH})_3$ . Potassium chlororuthenate ( $\text{K}_2\text{RuCl}_6$ ) is formed by igniting a mixture of the metal and potassium chloride in a current of chlorine. Ruthenium is converted into potassium ruthenate ( $\text{K}_2\text{RuO}_4$ ) by fusion with potassium nitrate and potassium hydroxide. This salt separates as black crystals from the yellow aqueous solution obtained by lixiviating the "melt." By passing chlorine or steam through the mother liquor, the volatile  $\text{RuO}_4$  is obtained as yellow crystals (1) which melt at about 25.5° C. and boil at about 100.8° C. Dilute acid acts upon potassium ruthenate to form potassium peruthenate ( $\text{KRuO}_4$ ). This reaction recalls the behavior of manganese compounds. This oxygen compound forms deep green aqueous solutions. Ruthenium dissolves slowly in aqua regia.



Neither the metal nor any of its compounds has any uses.

### RHODIUM

Symbol, Rh. Valence, III, IV. Atomic Weight, 102.91; Atomic Number, 45

Rhodium was discovered by Wollaston in 1803. In appearance it resembles aluminum. It has a density of 12.5 and melts at 1955° C. When heated strongly in oxygen, it forms the sesquioxide ( $\text{Rh}_2\text{O}_3$ ). The sesquioxide is basic and gives derivatives such as  $\text{Rh}_2(\text{SO}_4)_3 \cdot 12\text{H}_2\text{O}$  and  $\text{Rh}(\text{NO}_3)_3$ . The other oxides are  $\text{Rh}_3\text{O}_4$ ,  $\text{RhO}_2$ ,  $\text{Rh}_2\text{O}_5$  and  $\text{RhO}_3$ . Free chlorine attacks it and forms  $\text{RhCl}_2$  and  $\text{RhCl}_3$  (dark red). The latter forms  $\text{K}_2\text{RhCl}_6$  with potassium chloride. Ammonio-complexes of the type formed by cobalt are known. Example:  $\text{Rh}(\text{NH}_3)_6\text{Cl}_3$ . The pure metal in massive form is insoluble in acids and almost insoluble in aqua regia. When in a fine state of division, the metal slowly dissolves in aqua regia, in concentrated sulfuric acid, or in fused potassium hydrogen sulfate. Rhodium sulfate forms alums (*q. v.*) with alkali sulfates. The volatility of platinum is reduced by the addition of from 3 to 5 per cent of rhodium. Such an alloy, being harder and more durable than platinum, is especially adapted for making "platinum" crucibles.

### PALLADIUM

Symbol, Pd. Valences, I(?), II, III(?), IV. Atomic Weight, 106.7; Atomic Number, 46

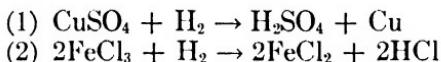
With the exception of platinum, palladium occurs in larger amounts than any other member of the family. It was discovered in 1803 by Wollaston. It is found associated with platinum in the

Urals and in Brazil. It is also found in the nickel ores of Sudbury, Ontario. It has a silvery appearance, is softer than platinum, has a density of about 11.4 and a melting-point of about 1555° C. which is the lowest melting-point of any of the platinum metals. The metal may be precipitated from solution in the form of a black powder.

Palladium usually exhibits a valence of 2 or 4. It unites with oxygen to form  $\text{PdO}$ ,  $\text{Pd}_2\text{O}_3$  and  $\text{PdO}_2$ . When heated, it combines directly with sulfur to form  $\text{PdS}$ . The halogens attack palladium and form the respective halides ( $\text{PdCl}_3$ ,  $\text{PdBr}_3$ , etc.). Strong concentrated acids, *e. g.*, hydrochloric acid, hot sulfuric acid, nitric acid, act upon the metal and form the chloride ( $\text{PdCl}_3$ ), the sulfate ( $\text{PdSO}_4$ ), and the nitrate ( $\text{Pd}[\text{NO}_3]_2$ ), respectively. From these reactions, we find that palladium is the most basic element of the family. Aqua regia acts vigorously upon it to form chloropalladic acid ( $\text{H}_2\text{PdCl}_6$ ).<sup>1</sup>

Solutions of palladous salts yield with ammonia T.S., a salmon-colored precipitate which is soluble in an excess of the reagent. Hydrochloric acid added to this solution produces a yellow precipitate of palladodisammime [ $\text{Pd}(\text{NH}_3)_2\text{Cl}_2$ ]. Solutions of palladous salts yield with potassium iodide T.S. a black precipitate of  $\text{PdI}_2$  which is visible in 1 to 500,000 parts of solution.

Finely divided palladium possesses to a greater degree than any other element the property of "occluding" or adsorbing large quantities of hydrogen. The finely divided metal ("palladium sponge") will adsorb at room temperature over seven hundred times its own volume of the gas. The action of hydrogen, which is very inactive at ordinary temperatures, is catalyzed by palladium. For example, it replaces copper from its salts (1), reduces ferric to ferrous salts (2) and converts chlorine into hydrogen chloride. Also, when a mixture of air and hydrogen is led over the powdered metal, the hydrogen is burned to water.



Palladium is used as an adsorbent for hydrogen in gas analysis. Its alloys with gold ("palau"), etc., resist corrosion and, therefore, are used for making jewelry, in dental practice, for coating reflectors, etc. The salts of the metal are sometimes used in photography. Also, metals are frequently coated with palladium.

### OSMIUM

Symbol, Os. Valences, II, III, IV, VI, and VIII. Atomic Weight, 190.2; Atomic Number, 76

Osmium was discovered by Tennant in 1803. This element has a density of 22.48 and is the heaviest known substance. It

<sup>1</sup> From this compound, potassium iodide precipitates black palladous iodide ( $\text{PdI}_2$ ) which is soluble in an excess of the reagent. This reaction is used as a test for palladium, but it is not as good as the formation of a reddish-brown precipitate by adding  $\alpha$ -nitroso- $\beta$ -naphthol to a solution of palladous chloride.

closely resembles zinc in color and luster and melts at 2700° C. Osmium occurs in platinum ores and in the form of an iridium alloy known as *osmiridium*.

Osmium forms several oxides, *viz.*, OsO, Os<sub>2</sub>O<sub>3</sub>, OsO<sub>2</sub>, and OsO<sub>4</sub>. Osmium tetroxide (OsO<sub>4</sub>) is analogous to ruthenium tetroxide (RuO<sub>4</sub>) and is by far the most important compound of the element. It is formed by heating powdered osmium in air or oxygen, or by treating the finely divided metal with aqua regia or nitric acid (either fuming or concentrated). It is volatile in steam; melts at 41° C.; and boils when heated to 134° C. The vapors are colorless, possess a disagreeable chlorine-like odor, and are very toxic and irritating to mucous membrane. Perhaps its greatest danger is its action on the eyes. Osmium tetroxide is sometimes called *osmic acid*. This is erroneous because the oxide does not form salts and its aqueous solutions are neutral in reaction. Aqueous solutions of osmium tetroxide are used for hardening and coloring (black) histological specimens from which microscopic sections are to be made.

In the massive condition, osmium is not attacked even by aqua regia. However, when finely divided, it is acted upon by concentrated inorganic acids. Osmium conforms to the group tendency to form double and complex salts with ammonia [(NH<sub>3</sub>)<sub>2</sub>OsCl<sub>6</sub>] and the halogens (K<sub>2</sub>OsCl<sub>6</sub>).

### IRIDIUM

Symbol, Ir. Valence, III, IV, and VI. Atomic Weight, 193.1; Atomic Number, 77

In 1803, Tennant discovered iridium. It is a white, hard, brittle metal having a density of 22.4. It is malleable at red heat and melts at 2350° C. In the massive state, it is nearly insoluble in aqua regia, but when finely divided, it dissolves slowly in this reagent. It also combines at red heat with oxygen, sulfur and phosphorus. When heated in the presence of sodium chloride, it reacts with chlorine to form the chloroiridate (Na<sub>2</sub>IrCl<sub>6</sub>). It is oxidized by strongly heating it with sodium hydroxide and potassium nitrate. If the fused mass is treated with aqua regia, a dark red solution of Na<sub>2</sub>IrCl<sub>6</sub> is obtained. Finely powdered iridium is a very powerful catalytic agent. Iridium imparts to its alloys its inherent property of resisting attack by powerful chemical reagents, *e. g.*, fluorine. Therefore, it is alloyed with 90 per cent of platinum and used for making crucibles, thermocouples, standard weights and measures, and other chemical apparatus. Alloys of iridium with either platinum or osmium are used to tip gold pens. Its salts are sometimes used in photography and its oxides for coloring china.

Iridium and its compounds closely resemble those of rhodium and nickel (*q. v.*). Three oxides of iridium are known, *viz.*, IrO, Ir<sub>2</sub>O<sub>3</sub> and IrO<sub>2</sub>. Ir<sub>2</sub>O<sub>3</sub> forms salts. Iridium forms four chlorides, *viz.*, IrCl, IrCl<sub>2</sub>, IrCl<sub>3</sub> and IrCl<sub>4</sub>. This element is more basic than acidic and possesses the group tendency to form double salts and complex compounds with the halogens and ammonia, Ir(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, Ir(NH<sub>3</sub>)<sub>4</sub>Cl<sub>2</sub>.

**PLATINUM**

Symbol, Pt. Valences, II, III, IV, VI. Atomic Weight, 195.23; Atomic Number, 78

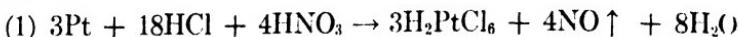
**History and Occurrence.**—The name of this element is derived from the Spanish *platina*, the diminutive of *plata*, meaning silver. This metal was first described by Watson (1750) and later studied by Marggraf and Bergman. Like gold, platinum occurs widely distributed in Nature, but in exceedingly small amounts. It is found alloyed with other metals, *e. g.*, ruthenium, rhodium, palladium, iridium, osmium, gold, silver, copper, iron, and in alluvial sands and gravels. The principal deposits are found in Canada, the U.S.S.R. and the Union of South Africa. The world production of platinum in 1946 is estimated to have been 576,000 troy ounces. The United States is the largest user of this metal.

**Physical Properties.**—Platinum is a grayish-white, lustrous metal. It can be welded at red heat and easily fused in the oxyhydrogen flame (melting-point, 1755°C.). It boils at 4300°C. Its ductility approaches that of gold and silver. Its usual malleability is markedly lessened by the presence of other metals, such as iridium, osmium, etc. It has a density of 21.45 and is fairly hard and tough. It is a good conductor of electricity and it has the lowest coefficient of expansion of all the metals. It may be sealed into glass. Molten platinum, like silver, adsorbs a large volume of oxygen. As the metal cools, oxygen is spasmodically liberated and gives rise to the phenomenon known as "spitting." When finely divided, platinum also adsorbs large quantities of gases, especially oxygen and hydrogen. These gases become so "activated" that they explosively combine with one another. Finely divided platinum often acts as an efficient catalyst. Its use in the form of platinized asbestos has been mentioned in connection with the contact process for making sulfuric acid. Since hydrogen diffuses through red hot platinum, it is unsafe to heat easily reducible substances in platinum vessels.

**Chemical Properties.**—Platinum forms two series of compounds, the *platinous* and the *platinic*, in which the metal exhibits valences of 2 and 4, respectively. It forms complex salts with ammonia.

Platinum is permanent in air and is not affected by hot or cold oxygen. It is not acted upon ordinarily by the common acids or by fused alkali carbonates. It is not attacked by dilute sulfuric acid, but the hot concentrated acid slowly acts on the metal and forms  $\text{Pt}(\text{OH})\cdot(\text{HSO}_4)_2$ . Neither hydrochloric nor nitric acid acts upon pure platinum, but aqua regia converts it into chloroplatinic acid ( $\text{H}_2\text{PtCl}_6$ ) (1). The addition of zinc to chloroplatinic acid reduces the latter to an extremely fine, hard, black powder known as *platinum black*. This substance will adsorb and activate large quantities of gases, such as hydrogen, oxygen, carbon monoxide, etc. Therefore, it is a powerful catalytic agent. Platinum is attacked by the halogens, sulfur, phosphorus, arsenic and carbon (smoky flame of burner). Fused sulfates and nitrates have some action upon it and

fused hydroxides and peroxides have a more pronounced action. Platinum will form alloys with low melting-point metals, such as lead. The chlorides of magnesium and lithium will materially injure platinum.



**Commercial Manufacture.**—Much of the platinum is obtained as a secondary metal during the refining of Cu, Pb, Ni, etc. The platinum-bearing sands and gravels are levigated to obtain a residue containing from 60 to 80 per cent of platinum and associated metals. This is digested with aqua regia, which slowly dissolves the platinum and allied metals, filtered, and the filtrate made almost neutral with a solution of calcium hydroxide. This precipitates most of the iron, copper, rhodium, and iridium and some of the palladium which are filtered off and the solution evaporated to dryness. The dried material is heated to about 125° C. and extracted with water and hydrochloric acid. Ammonium chloride is added to the solution to precipitate the difficultly soluble ammonium chloroplatinate ( $[\text{NH}_4]_2\text{PtCl}_6$ ). The precipitate is dried and heated to redness to decompose the salt into a porous, metallic mass called *spongy platinum*. The massive or compact form of the metal is obtained by hammering the spongy metal at red heat or by melting it in a refractory crucible which is heated by the oxyhydrogen flame. The melted platinum is then cast into bars weighing from 2 to 5 kilos.

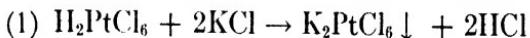
**Uses.**—The physical properties of platinum, *viz.*, malleability, ductility and high melting-point, together with its chemical inactivity, *viz.*, resistance to acids and fused alkali carbonates, make it especially suited for making crucibles, dishes, wire, foil and other physical and chemical apparatus. It is used for plating other metals and for making jewelry. In a finely divided form, platinum is used extensively as a catalyst.

### PLATINUM COMPOUNDS

Four oxides of platinum are known, *viz.*,  $\text{PtO}$ ,  $\text{Pt}_2\text{O}_3$ ,  $\text{PtO}_2$  and  $\text{PtO}_4$ .  $\text{PtO}$  and  $\text{PtO}_2$  are black powders obtained by gently heating the respective hydroxides. Platinous chloride ( $\text{PtCl}_2$ ) is formed by passing chlorine over finely divided platinum heated between 240° and 250° C. It is a gray-green insoluble powder. It dissolves in hot hydrochloric acid to form *chloroplatinous acid* ( $\text{H}_2\text{PtCl}_4$ ). Platinum chloroplatinite is used in “toning” solutions for making platinum photographic prints. Potassium platinocyanide [ $\text{K}_2\text{Pt}(\text{CN})_4 \cdot 3\text{H}_2\text{O}$ ] and barium platinocyanide [ $\text{BaPt}(\text{CN})_4 \cdot 4\text{H}_2\text{O}$ ] are yellow, strongly fluorescent powders. The barium salt is used for coating screens on which the shadows of objects interfering with the Roentgen rays are observed during fluoroscopic examination.

When platinum is dissolved in aqua regia and the solution evaporated with hydrochloric acid to expel nitric acid, brownish-red, deliquescent crystals of chloroplatinic acid ( $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$ ) are

formed. A solution of chloroplatinic acid precipitates sodium, potassium and ammonium ions from their solutions. Sodium chloroplatinate ( $\text{Na}_2\text{PtCl}_6$ ) is not only the most soluble of the three salts but also differs from potassium and ammonium chloroplatinates by being soluble in diluted alcohol. This difference in solubility has been made use of in effecting the quantitative separation of sodium and potassium (1). As previously noted, zinc reduces



chloroplatinic acid to a fine powder called platinum black. When asbestos or other fibrous material is saturated with a solution of chloroplatinic acid and then strongly heated, the acid is decomposed and leaves the finely divided platinum throughout the mass. This mass is then said to be "platinized" (platinized asbestos). Platinic chloride ( $\text{PtCl}_4$ ) is made by heating chloroplatinic acid in a current of chlorine at  $360^\circ \text{ C}$ . This compound unites with water to form  $\text{H}_2\text{PtCl}_4\text{O} \cdot 4\text{H}_2\text{O}$ . With bases, it forms platinic hydroxide [ $\text{Pt(OH)}_4$ ], which interacts with bases to give platinates. Platinous sulfide ( $\text{PtS}$ ) and platinic sulfide ( $\text{PtS}_2$ ) are precipitated from the aqueous solutions of the corresponding chlorides by hydrogen sulfide. These brownish-black powders are soluble in the alkali sulfides.

A characteristic test for platinum depends upon the formation of a reddish-brown coloration when a solution of  $\text{PtCl}_4$  is treated with a solution of potassium iodide. A black precipitate of platinic iodide may be formed also. An excess of the KI produces  $\text{K}_2\text{PtI}_6$ , which is a brown, slightly soluble, and unstable compound. When solutions of the chlorides of the platinum metals are treated with sodium formate in neutral solution, the free metals are liberated. Sometimes the action is very slow and a point of near neutrality must be maintained.

## CHAPTER XLVIII

### THE INERT GASES

DURING the years 1893–1895, Lord Rayleigh made a series of very accurate determinations of the densities of gases. He noticed that nitrogen isolated from the atmosphere was always heavier than the nitrogen he prepared from compounds, such as ammonium nitrite, urea and the oxides of nitrogen. A constant difference in density of 0.065 ( $H = 1$ ) was too great to be considered as an experimental error by such a careful investigator as Rayleigh, so he was led to suspect the presence of some new gas in the atmosphere. In 1785, Cavendish came to the same conclusion after eliminating the ordinary components of air and finding a small, inactive gaseous residue that would not unite with oxygen on sparking over a concentrated solution of potassium hydroxide. Cavendish did not pursue the subject further, but Rayleigh repeated the experiment in conjunction with Sir William Ramsay and, on removal of the last traces of nitrogen with red hot magnesium, found that the residual gas gave a spectrum different from that of any known element. Ramsay named the new element *argon* (Greek, meaning *lazy*) because of its complete chemical inertness. Ramsay and Travers then fractionated large quantities of liquid air and discovered neon, krypton and xenon. Ramsay also found helium in crude liquid argon, but a further search of 120 tons of liquid air failed to reveal the presence of any other new gases.

#### **HELIUM**

##### *Helium, U. S. P. XIII*

Formula, He. Atomic Number, 2. Atomic Weight, 4.003

**Physical Properties.**—Helium is a colorless, tasteless, odorless gas with a density of 0.1380 (air = 1). Helium is the lightest of all gases with the exception of hydrogen, and has a buoyancy of 92.6 per cent of the latter gas. A liter of the gas at standard temperature and pressure weighs not less than 174.5 mg. and not more than 232.5 mg. Helium is practically insoluble in water. Experiments recently carried out show that it is also insoluble in blood (nitrogen, however, is much more soluble).

**Chemical Properties.**—Helium is chemically inert. It does not support combustion and will prevent hydrogen from burning when mixed with it.

**Official Tests for Identity.**—A burning splinter of wood is extinguished in an atmosphere of helium. Mixtures of hydrogen and helium are neither inflammable nor explosive when oxygen is excluded.

**Commercial Manufacture.**—In 1895, helium was shown to be present in the air. Ramsay found the amount to be 0.0004 per cent by volume, or 0.000056 per cent (1 part in 1,800,000 parts) by weight. It has been estimated that a total of  $58 \times 10^{12}$  cm. of helium exists in the earth's atmosphere. The gas is found in small percentages dissolved in many spring waters and mixed with the gases issuing from these springs. Helium has been detected in volcanic gases, in natural gases and occluded in all radioactive minerals. Natural gases have been found with a helium content of 2 per cent; the average content of the wells in a zone comprising Texas, Oklahoma, Kansas, Illinois, Ohio, Pennsylvania and New York is only 0.5 per cent. Natural gas wells all over the rest of the world contain very small percentages of helium. The wells richest in helium are those in Texas, Oklahoma and Kansas. These wells give the United States a monopoly as far as production on a commercial scale is concerned. The separation of helium from the other gases with which it is associated in natural gas is accomplished in a modified form of liquid air machine. Helium approaching a purity of 100 per cent can be obtained in the final stage of adsorbing the remaining quantities of contaminating gases in charcoal at the temperature of liquid air.

Helium resisted all attempts at liquefaction until 1908, when the efforts of H. K. Onnes were successful. Expansion of compressed helium at the temperature of liquid hydrogen resulted in liquefaction. Onnes found liquid helium to be colorless and very mobile; the liquid boils at  $-268.9^{\circ}\text{C}.$  and has a density of 0.147 at  $-270.8^{\circ}\text{C}.$  The critical temperature of helium is given as  $-267.9^{\circ}\text{C}.$ ; the critical pressure is 2.26 Å. It is interesting to note that at the temperature of liquid helium, the electrical resistance of metals drops practically to zero; the metals become "superconductors."

**Pharmaceutical Preparations and Uses.**—1. *Helium* (Helium), U. S. P. XIII.—Helium contains not less than 95 per cent by volume of He, the remainder consisting mainly of nitrogen. Helium has been used in respiratory diseases, for mixing with anesthetic gases and for the prevention of "bends" in underwater workers.<sup>1</sup> Other uses suggested for helium include the cooling of electrical equipment, the preservation of food, and the formation of an inert atmosphere for carrying out chemical reactions which are sensitive to air.

## NEON

Ramsay and Travers first obtained neon (Greek, meaning *new*) by fractional distillation of liquid air. The gas is colorless, odorless and chemically inert like the other members of this group. The density is 0.6962 (air = 1). Neon can be condensed to a liquid which has a specific gravity of 1.204 at its boiling-point of  $-245.9^{\circ}\text{C}.$  The critical temperature of the gas is  $-228.7^{\circ}\text{C}.$ , and the critical pressure is 25.9 Å.

<sup>1</sup> Chemical Industries, 57, 470 (1945)

The element is readily identified by a characteristic spectrum showing many bright lines in the red and in the orange portions. When an electrical discharge is sent through neon under diminished pressure, a brilliant orange-red glow results. Extensive use of this property is made for advertising purposes. Neon-filled glass tubes bent in the shape of letters and various designs make attractive signs and create unique decorative effects. The light has considerable penetrating power for fogs, so neon lamps have been installed in lighthouses, at airports and along passenger and air mail routes.

### ARGON

The discovery of argon has been discussed at the beginning of this chapter. By far the most abundant and the most widely distributed of the inert gases, argon is found in the air (0.94 per cent by volume), in natural gas, occluded in minerals and dissolved in the oceans and in all fresh waters. It has been calculated that about 800,000,000 pounds of argon are contained in the air above each square mile of the surface of the earth.

Argon is a colorless, odorless gas with a density of 1.378 (air = 1). Liquid argon boils at  $-185.7^{\circ}\text{C}$ . and has a specific gravity of 1.402 at its boiling-point. The critical temperature of the gas is  $-122.4^{\circ}\text{C}$ ., the critical pressure is 48 A. Solid argon melts at  $-189.2^{\circ}\text{C}$ .

The abundance of the gas, and the fact that it is a by-product of several liquid air processes, insure a low cost of production. At present, it is filled into electric lights to slow up the blackening of the bulbs and to secure longer life for the filaments. Fluorescent tubes used for lighting purposes contain a mixture of mercury vapor and argon at a low pressure (3 mm.).

### KRYPTON

Ramsay and Travers isolated krypton (Greek, meaning *hidden*) in liquid air residues from which argon had been separated. Ramsay found 1 volume of krypton to be present in 20,000,000 volumes of air; the present value is 1 in 1,000,000. Small quantities of krypton are found in the gases issuing from thermal springs and occluded in certain minerals.

Like the other members of the family, krypton is a colorless, odorless gas with a density of 2.8675 (air = 1). The critical temperature is  $-63^{\circ}\text{C}$ ; the critical pressure is 54 A. Liquid krypton has a specific gravity of 2.155 at its boiling-point of  $-152.9^{\circ}\text{C}$ . Solid krypton melts at  $-157^{\circ}\text{C}$ . A mixture of this gas and xenon is used in tubes to produce an intense light of short duration for high speed photography.

### XENON

The isolation of xenon by the fractionation of liquid air was accomplished by Ramsay and Travers. The name is derived from a Greek word, meaning *the stranger*. Xenon is the least abundant of

the inert gases, for there is only 1 volume of the gas in 11,000,000 volumes of air. The gas has a density of 4.525 (air = 1), a critical temperature of 16.6° C., and a critical pressure of 58.2 A. Liquid xenon boils at -107.1° C.; its specific gravity is 3.06 at -109°. Solid xenon melts at -112° C.

### RADON

In 1901, Dorn recognized the presence of a new inert gas given off by radium salts and their aqueous solutions. Rutherford and Soddy succeeded in liquefying the emanation; Ramsay and Collie demonstrated its possession of a characteristic spectrum. Ramsay called the gas *niton*, but this has since been changed to *radon*.

The gas occurs in all radium minerals and in small quantities in any waters that have come into contact with the minerals. Radon is much more soluble in certain organic solvents. Directly after the preparation of an aqueous solution of a radium salt, the rate of accumulated radon increases rapidly for a few days and then goes up more slowly, until a constant, maximum rate is reached. Radon itself undergoes radioactive disintegration but does not enter into any chemical reactions.

The density of radon is 7.525 (air = 1). The gas has a critical temperature of 104° C. and a critical pressure of 62 A. Liquid radon boils at -61.8° C. and has a specific gravity of 4.4 at its boiling-point; solid radon melts at -71° C.

Radon is used in the treatment of cancer. The emanation is collected in small glass or gold tubes, and these are applied to the area to be treated. There is an economic advantage in the use of radon instead of a radium salt. Carelessness on the part of hospital staffs or patients has sometimes resulted in the loss of radium salts and a consequent heavy financial loss. With the use of radon, the radium salt need never be removed from the room in which the gas is collected.

## CHAPTER XLIX

### RADIOACTIVITY AND THE RADIOACTIVE ELEMENTS

IN 1878, Sir William Crookes discovered that when an electric discharge was passed through an evacuated tube (Crookes' tube) the rays coming from the cathode (cathode rays) produced a greenish-yellow fluorescence in the glass posteriorly to the anti-cathode. These rays were markedly different from the ordinary light rays in that they did not illuminate, could be deflected from their straight course by a magnet and caused certain chemical substances placed inside the discharge tubes to fluoresce. In 1895, while working in his laboratory with discharge tubes, Roentgen quite accidentally discovered that a fluorescent screen became luminous when placed near these tubes. He observed also that these radiations affected photographic plates and penetrated paper, flesh, wood and other substances opaque to ordinary light. Roentgen's discovery of the *x-ray* stimulated research in these fields and focussed attention on those phenomena which led a year later to the discovery of radioactivity.

The fluorescence of glass subjected to cathode rays led several scientists to investigate those chemical substances which were rendered fluorescent by visible light. In 1896, Prof. H. Becquerel, a noted French physicist, exposed a photographic plate to phosphorescent uranium potassium sulfate that had been wrapped in black paper, and found that the plate was fogged by rays emanating from this double salt. Furthermore, he observed that the air about the radioactive compound was conductive to electricity (ionized) as evidenced by the collapse of the leaves of a charged electroscope. Rutherford showed that this effect was due to the production of ions in the gas through which the radiations passed. Some time later, Mme. Curie conducted extensive researches to determine what elements and their compounds possessed this property of radioactivity. She found only one other element, thorium, comparable in this respect to uranium. After she had established the fact that the radioactivity of a compound was proportional to the quantity of the element (thorium or uranium) present in the compound regardless of how it was combined, she then observed that the radiations from *pitchblende* ( $\text{U}_3\text{O}_8$ ) were between four and five times more intense than that of metallic uranium, of which it contained only about 50 per cent. Having faith in her hypothesis, she quite logically concluded that pitchblende contained, besides uranium, one or more radioactive substances and set about isolating them.

The Austrian government provided her with a large quantity of the residues left after the recovery of the uranium from pitchblende mined at Joachinenthal, Bohemia. These residues were found to

be from three to five times as radioactive as uranium itself. From them, Mme. Curie first isolated an element that was much more radioactive than uranium, and which she named *polonium* in honor of her native country, and, in 1898, the element *radium*, which she found to be one million times more active than uranium. Since then a number of naturally radioactive substances have been discovered. They are as follows:

Atomic No.	Principal element of this atomic number
92	Uranium, UII, U <sup>238</sup> . . . . . U
91	UX <sub>2</sub> , UZ, Pa . . . . . Pa
90	UX <sub>1</sub> , Io, UY, RdAc, Th, RdTh . . . . . Th
89	Ac, MsThII . . . . . Ac
88	Ra, AcX, MsThI, ThX . . . . . Ra
87	
86	RaEm, AcEm, ThEm or Rn, An, Tn . . . . . Rn
85	
84	RaA, RaC', RaF (polonium), AcA, AcC', ThA, ThC' . . Po
83	RaC, RaE, AcC, ThC . . . . . Bi
82	RaB, RaD, RaG, AcB, AcD, ThB, ThD . . . . . Pb
81	RaC'', AcC'', ThC'' . . . . . Tl

The radioactive elements are arranged into sequences or families: the uranium series, the thorium series, and the actinium series. According to this (counting isotopes separately) there are about forty radioactive elements whose existence has been demonstrated.

All elements having atomic weights above 222 are radioactive. Potassium, rubidium, samarium, and neodymium also possess this property to some degree. All radioactive compounds have the common property of emitting rays or particles which affect a photographic plate protected from visible light and also cause the discharge of electrified bodies. When an element is designated as being "radioactive," it implies that such an element is unstable and is undergoing spontaneous decomposition or rather disintegration at a definite and computable rate into other elements of the same or lower atomic weight. This disintegration process is invariably accompanied by the emission of radiations or "rays" that have been proven to be of three kinds. In 1899, Rutherford showed that the radiation from uranium was not a single ray but, rather, was composed of two kinds of rays which he called the *alpha*- and *beta*-rays, respectively. They differed from one another in penetrating power. Later, Villard discovered a still more penetrating ray which he named the *gamma-ray*. In many cases these elements disintegrate so slowly as not to seem to change at all. Yet they do so with the evolution of an enormous quantity of energy. Radium, for example, gives out heat and light continuously and without being in any visible way consumed or altered. It appears to be performing the scientifically impossible act of producing energy out of nothing. From this it follows that the elements resulting from the radioactive change have less internal energy.

1. *The Alpha-rays*.—Of the three rays, the *alpha*-rays or particles are the least penetrating. They are stopped by a sheet of paper or

a few centimeters of air. Each particle is really the nucleus of a helium atom and, therefore, has a mass of 4. It carries two positive charges. These rays travel with an average velocity of 18,000 miles per second and ionize the air in their paths. They are deflected by a strong magnetic field. When the *alpha*-rays are received upon a zinc sulfide screen, minute flashes of light may be observed equal to the number of *alpha* particles which may be counted over a given time. Soddy and Ramsay identified the helium gas given off by radium compounds and measured the rate of its production.

2. *The Beta-rays.*—Becquerel and Kaufmann showed that the *beta*-rays consist of negative charges of electricity (electrons). Each of these particles has an apparent mass of  $185\sigma$  that of a hydrogen atom and is projected with a velocity that may approach that of light. Giesel, Curie and Becquerel showed that *beta*-rays were deflected by a magnetic field in a direction opposite to that observed for the *alpha*-rays. The *beta*-rays are electrons, identical with the cathode-rays and will penetrate thin layers of metal and other substances.

3. *The Gamma-rays.*--These rays are not affected by magnetic forces and appear to be of the same character as the very short electromagnetic waves called *x*-rays. The *gamma*-rays may be observed either from those substances which emit *alpha*- or *beta*-rays. They are much more penetrating than either the *alpha*- or the *beta*-rays, and will pass through great thicknesses of metal or other material of low atomic weight without complete absorption.

### ARTIFICIAL PRODUCTION OF RADIOACTIVE SUBSTANCES

In 1919 Rutherford found that alpha particles from radioactive substances could, upon striking the nucleus of certain elements, notably nitrogen, transmute them by the immediate ejection of a proton. In 1932 Cockcroft and Walton found that protons moving under the force of several hundred kilovolts could also produce *immediate* transmutation. In January, 1934, I. Curie and F. Joliot discovered that the action of alpha particles on boron produced transmutation which, instead of being instantaneous, gave an intermediate product which slowly changed to the final product, carbon, accompanied by the emission of positrons. This gradual process of transmutation is known as artificial or *induced* radioactivity. A variety of agents have been found effective in the case of many elements. Practically all of the elements have been found to have radioactive isotopes, some of them have several species, which can be produced by bombardment of neutrons, deuterons, or protons. The latter two must be accelerated by some suitable electric device such as the cyclotron, capable of giving very high voltage. Neutrons, being neutral particles, cannot be accelerated in an electric field, but are the direct product of many of the nuclear changes.

Protons and deuterons under high electrical propulsion as well as natural alpha particles can act on the lighter elements. Neutrons

produced from *alpha*-ray bombardment are universal in their action on heavy as well as light elements.

Among the most important of the artificial radioactive elements are Na<sup>24</sup> and P<sup>32</sup>, the former changing with a half-life of fifteen hours, the latter of fourteen days. Na<sup>24</sup> emits electrons and gamma radiation more penetrating than that from RaC and may become a serious competitor with Ra in therapeutic use. P<sup>32</sup> has been used as a radioactive indicator to trace the location and migration of phosphorus compounds both in animals and in plants, and as a therapeutic agent by intravenous injection. Carbon 14 (C<sup>14</sup>) having a half-life of about ~~1000~~ years and iodine 131 (I<sup>131</sup>) with a half-life of eight days are used extensively in biological and chemical studies.

### RADIUM

Symbol, Ra. Valence, II. Atomic Weight, 226.05;  
Atomic Number, 88

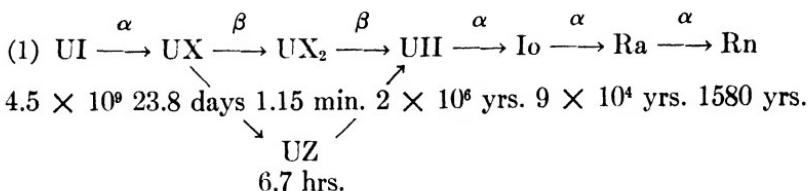
In 1898, M. and Mme. Curie isolated this metallic chemical element from pitchblende, a uranium mineral. It was named *radium*, from the Latin *radius*, a ray, because of its intense radioactivity.

In Nature, this element is found very sparingly associated with uranium. It occurs also in some natural spring waters. The residues remaining after extracting the uranium from Bohemian pitchblende, provide most of the European radium. A potassium uranium vanadate (*carnotite*) found in Utah and Colorado was formerly the source of some of the radium used in this country. Most of the world's present supply of radium has had its origin either in the uranium deposits in the Belgium Congo in Central Africa or at Great Bear Lake in the Canadian Northwest Territory. Although radium occurs more plentifully than any other therapeutically used radioactive element, its extreme scarcity is evidenced by the fact that Mme. Curie obtained only a fraction of a gram of the chloride from 1 ton of uranium residues.

In general, the properties of radium resemble those of the alkaline earths, especially barium, from which it is separated by the fractional crystallization of its halogen salts, usually the bromide. Its spectrum is characteristic. Its atomic weight, together with its analytical reactions and chemical behavior, place it in Group II.

Radium is a product of the disintegration of uranium (1). The discharge of *alpha*-rays over an estimated period of 4.5 million years changes one-half of uranium into UX<sub>1</sub>, which, however, breaks down at such a rate that in 23.8 days it is about one-half gone, etc. The result is that at any time there are very small quantities of UX<sub>1</sub>, UX<sub>2</sub> or UZ present, but more of UII, Io and Ra. The times given (half-change periods) are not those required for the substance to disappear, but only to drop to one-half of its original amount. After 76,000 years of *alpha*-ray emanation, one-half of ionium is completely changed to radium. The designated

disintegration changes are always accompanied by the emission of electrons or helium nuclei (beta or alpha particles).



Shortly after the discovery of radium, Dorn observed that radium emanation is a gas which is chemically inactive and, therefore, resembles the inert gases. Ramsay and Gray named this gas *niton*, but it is now called *radon*. It was found that this gaseous element is slightly soluble in water and very soluble in fixed oils, especially olive oil. Carbon, petrolatum and some other organic substances hold this gas very well. Solutions of this gas give off *alpha*-rays, but in 3.85 days (half period only) undergo radioactive disintegration into radium-A (half-change period = 3 minutes), then to radium-B (half-change period = 26.8 minutes) and then to radium-C (half-change period = 19.5 minutes) which gives off *alpha*-, *beta*- and *gamma*-rays. The next disintegration product is radium-D (half-change period = 22 years) which changes to short-lived radium-E (half-change period = 5 days) and then to radium-F or polonium. The emission of *alpha*-rays for 136 days (half-change period) by polonium yields the final decomposition products, RaG (U lead, UPb).

**Uses.**—The radiations from radium, like the Roentgen rays, are capable of destroying living cells. This property was unknown until 1901, when Becquerel received a severe burn from a tubed sample which he had carried around for several weeks in his waistcoat pocket. The blood vessels and blood-making organs of the body are especially susceptible to the action of radium rays. Radium, for therapeutic purposes, is applied in the form of one of its salts (usually the bromide, RaBr<sub>2</sub>) or as the emanation (radon). (Radium salts or radium emanation are used to arrest and cure malignant growths. When small gold capsules of radium emanation are buried in cancer tissue, they cause the degeneration of the cancer cells with subsequent reduction in the size of the growth.) It has been of value in the treatment of enlarged thyroids, cataracts and hardened scar tissue.

**Measurement of Radioactivity.** A measure of the radioactivity of a substance may be obtained by comparing the rate at which it discharges a charged gold leaf electroscope to the rate of discharge caused by some compound of known radioactivity. The value of radium preparations is dependent upon the amount of radium present in them. The United States Bureau of Standards offers the following method of determination, *viz.*: By measuring the rate of discharge of an electroscope by the *gamma*-rays that have passed

through a sheet of lead 1 cm. thick. The units employed for expressing radioactivity are of two kinds, *viz.*: (1) Those that express actual quantity of radium present as such; and (2) those that express the emanation concentration. The quantity of radium present in a compound may be expressed in (a) milligrams or decimals thereof, or (b) in micrograms or decimals thereof. A microgram is 0.001 part of a milligram. The amount of emanation may be designated in: (a) Curies, millicuries or microcuries; the curie is the maximum quantity of emanation emitted by 1 gram of radium or, in other words, that quantity of emanation resulting when 1 gram of radium is in equilibrium with its disintegration products. (b) A Maché unit is equal to  $\frac{1}{2700}$  of 1 microcurie of radium emanation per liter (of water).

Of late years so-called "counting" methods are employed for the detection and measurement of radioactive substances. By this method the actual number of particles or rays emitted can be counted by use of the Geiger-Müller electrical counter. This enables the detection and determination in very small quantities.

### ATOMIC FISSION

After the discovery of the neutron by Chadwick in 1932 it was natural to try it as a bombarding agent of the various elements. It was found that on account of its having no charge, it could enter the nuclei of the heavy elements as readily as those of the light ones. Fermi bombarded the element Uranium with neutrons and found a multiple emission of beta particles, which he interpreted as the successive production of elements 93, 94, 95 and 96 by *beta-ray* change. In January, 1939, however, Hahn and Strassman proved the presence of Barium in the bombarded Uranium. This discovery led to the idea of fission—by which is meant that the element Uranium is split by the entrance of a slow neutron and then emits two or three high-speed neutrons and several beta particles.

The two products of fission are elements distributed in pairs all the way from those with atomic number 30 up to about 60. The sum of the atomic numbers of each pair must be equal to that of Uranium 92. This gives some 30 or 40 fission products which are isotopes of known elements in the range mentioned. Some of these isotopes were previously known; others are new. In the Uranium pile they are produced in much larger quantities than have hitherto been available either in natural radioactive elements or by production in the cyclotron. They are now available for practical use. Some of them are useful in therapy, others as tracer elements.

It was found by Nier that it is the isotope U<sup>236</sup>, which occurs in the natural mixture to the extent of about 0.7 per cent, which produces rapid and multiple fission. This property has been used in the production of the atomic bomb.

By mixing Uranium and Graphite in a suitable geometrical arrangement, a self-sustaining chain reaction is achieved which

is made use of at Pasco, Washington, in operating a pile for the production of a new element, No. 94, called Plutonium, which is also like U<sup>235</sup>, fissionable and has the advantage of easy chemical separation from Uranium; whereas, the separation of U<sup>238</sup> and U<sup>235</sup> is difficult and expensive.

It is possible that the atomic energy produced by fission may be utilized for industrial power production. One great difficulty consists in the large amount of very penetrating radiation which is released by fission. To protect against this requires such a large mass of shielding that the use of atomic energy for any small scale use seems to be prohibited. Also the radioactive gases that are produced must be kept confined to avoid serious contamination of the surrounding atmosphere.

Elements 43, 61, 85 and 87, which have never been found in Nature, have recently been produced by bombardment of neighboring elements. The isotopes which are thus produced and have been found radioactive have been given the following names:

43	Technitium
61	Formerly Illinium and has not been renamed
85	Astatine
87	Francium

### THORIUM

Symbol, Th. Valence, IV. Atomic Weight, 232.12; Atomic Number, 90

In 1815, Berzelius extracted what he thought to be a "new earth" from several rare Swedish minerals. He named the substance *thoria* after the Scandinavian god, Thor. His new element was later found to be a basic yttrium phosphate. However, in 1828, he discovered thorium in the mineral *thorite* (ThSiO<sub>4</sub> or ThO<sub>2</sub>.SiO<sub>2</sub>) which occurs in small amounts at Lérön.

The principal source of thorium is the monazite sands of Brazil, India and North and South Carolina. It is found also in the mineral *thorianite*, a mixture of thorium dioxide and uranium oxides.

Thorium is a soft and ductile metal having a density of 11.2. It melts at 1845° C. and is only slowly attacked by acids. Aqua regia dissolves it. This element is decidedly basic in character and, in chemical behavior, it closely resembles the rare-earth elements. Thorium forms a complete series of single [Th(SO<sub>4</sub>)<sub>2</sub>.4H<sub>2</sub>O] and double salts [MgTh(NO<sub>3</sub>)<sub>6</sub>.8H<sub>2</sub>O] in which it is quadrivalent.

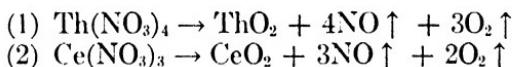
Thorium is a radioactive element and, like uranium, is the parent element of a series of disintegration products, such as mesothorium I (half-change period = 6.7 years), mesothorium II (half-change period = 6.2 hours), radiothorium (half-change period = 1.9 years), thorium X (half-change period = 3.64 days), thorium emanation (half-change period = 54.5 seconds), thorium A (half-change period = 0.14 second), thorium B (half-change period = 10.6 hours),

thorium C (half-change period = 60.8 minutes), thorium C' (half-change period =  $10^{-11}$  seconds), thorium C<sup>II</sup> (half-change period = 3.2 minutes) and thorium D which is thorium lead and is not radioactive. The disintegration stages are all going on at the same time. In the steady state, the amount of any product present varies directly as its half-period.

**Uses.**—Thorium was introduced into medicine very soon after radium. Soluble thorium salts very closely resemble alum in their local astringent and irritant properties. The nitrate [Th(NO<sub>3</sub>)<sub>4</sub>.4H<sub>2</sub>O] and sulfate [Th(SO<sub>4</sub>).4H<sub>2</sub>O] have been used in the treatment of diarrhea. The non-toxic double salt, sodium and thorium citrate, is opaque to Roentgen rays and, because it is excreted by the kidneys, a neutral 10 per cent aqueous solution is sometimes used for diagnostic purposes in pyelography and cystography.

Mesothorium is used in the manufacture of luminous paints. The radioactive substance is mixed with small crystals of zinc sulfide and a "binder," and painted upon clock and watch dials, electric pull switches, etc. The zinc sulfide fluoresces when acted upon by the *alpha*-rays of the radioactive substance.

Thorium nitrate is used in making Welsbach mantles. The framework of the mantle is woven from the very fine and strong fibers of grass cloth (*Boehmeria nivea*). This is saturated with a solution containing thorium nitrate and cerium nitrate in the proportions of 99 to 1, moulded to the desired shape and dried. The organic matter is burned away in a Bunsen flame and the nitrates are decomposed to oxides (1) (2).



The oxides retain the shape of the cloth and, in order to prevent breakage, the delicate mantle is dipped in collodion and dried. These oxides hasten combustion by virtue of their contact action, and thus produce a much higher temperature on their surfaces than is observed for the rest of the flame. For the same amount of illuminating gas, the Welsbach mantle gives about four times as much light as the ordinary "tip-burner."

With the actual displacement of Welsbach mantles by incandescent electric lights, the use of thorium in gas mantles has decreased and but little by-product mesothorium is now obtained from this source. It is not profitable to extract mesothorium alone.

Thorium dioxide is used as a radiopaque medium in a 25 per cent colloidal solution. It flocculates forming a surface coating on mucous membranes, making it useful for *x-ray* pictures of intestinal, stomach and bladder walls.

MENDELEEFF'S PERIODIC TABLE OF ELEMENTS (Revised 1947)<sup>1</sup>

Perriods	Group I	Group II	Group III	Group IV	Group V	Group VI	Group VII	Group VIII	Group 0
I	H 1 1.008								He 2 4.003
II	Li 3 6.940	Be 4 9.02	B 5 10.82	C 6 12.010	N 7 14.008	O 8 16.0000	F 9 19.00		Ne 10 20.183
III	Na 11 22.997	Mg 12 24.32	Al 13 26.97	Si 14 28.06	P 15 30.98	S 16 32.066	Cl 17 35.457		A 18 39.944
	A	B	B	A	B	A	B	A	
Even Series	K 19 39.096	Ca 20 40.08	Sc 21 45.10	Ti 22 47.90	V 23 92.91	Cr 24 52.01	Mn 25 54.93	Fe 26 55.85	Ni 28 58.94
Odd Series	Cu 29 63.54	Zn 30 65.38	Ga 31 69.72	Ge 32 72.60	As 33 74.91	Se 34 78.96	Br 35 79.916		Kr 36 83.7
Even Series	Rb 37 85.48	Sr 38 87.63	Y 39 88.92	Zr 40 91.22	Cb 41 92.91	Mo 42 95.95	Ma 43 101.7	Ru 44 102.91	Rd 46 106.7
Odd Series	Ag 47 107.880	Cd 48 112.41	In 49 114.76	Sn 50 118.70	Sb 51 121.76	Te 52 127.61			Xe 54 131.3
	Cs 55 132.91	Ba 56 137.36	La 57 138.92	Ce 58 140.13					
			Also rare-earth metals 59 to 71*	Hf 72 178.6	Ta 73 180.88	W 74 183.92	Re 75 186.31	Os 76 190.2	Ir 77 193.1
									Pt 78 195.23
VI	Au 79 197.2	Hg 80 200.61	Tl 81 204.39	Pb 82 207.21	Bi 83 209.00	Po 84 209.00	-85		Rn 86 222
VII	-87	Ra 88 226.05	Ac 89 .	Th 90 232.12	Pa 91 231	U 92 238.07			
Formulas of Oxides Formulas of Hydrides	RO RH	RO RH;	RO <sub>3</sub> RH;	RO <sub>4</sub> RH;	RO <sub>3</sub> RH;	RO <sub>4</sub> RH	RO <sub>4</sub>	RO <sub>4</sub>	
*Pr 59 140.92	Nd 60 144.27	Eu 61 150.43	Eu 63 152.0	Gd 64 156.9	Tb 65 159.2	Dy 66 162.46	Ho 67 164.94	Er 68 167.20	Tm 69 169.4
									Yb 70 173.04
									Lu 71 174.98

<sup>1</sup> Arranged by Sneed.

## ELECTROMOTIVE SERIES OF THE METALS

1. Cesium	8. Calcium	15. Iron	22. Arsenic
2. Rubidium	9. Magnesium	16. Cobalt	23. Bismuth
3. Potassium	10. Aluminum	17. Nickel	24. Antimony
4. Sodium	11. Manganese	18. Tin	25. Mercury
5. Lithium	12. Zinc	19. Lead	26. Silver
6. Barium	13. Chromium	20. Hydrogen	27. Platinum
7. Strontium	14. Cadmium	21. Copper	28. Gold

## METHOD OF CALCULATION FOR ISOTONIC SOLUTIONS

**Step 1.**—Multiply the amount of the ingredient, or ingredients given in the prescription by the sodium chloride equivalents for these ingredients given in the table.

**Step 2.**—Add the products in Step 1.

**Step 3.**—Multiply the weight of the prescription by 0.014 to determine how much sodium chloride is needed alone for an isotonic solution. (A 1.4 per cent sodium chloride solution is isotonic with the lachrymal fluid.)

For a prescription in the apothecary system:

Fluidounces  $\times$  455 gr. = weight.

For a prescription in the metric system.

Cubic centimeters  $\times$  1 Gm. = weight.

**Step 4.**—Subtract the equivalent amount of sodium chloride obtained from addition in Step 2, from the amount of sodium chloride alone as calculated in Step 3. The difference is the amount of sodium chloride to be added to the prescription to make it isotonic.

**Step 5.**—(This step is used ONLY when an ingredient other than sodium chloride, *i. e.*, boric acid, dextrose, etc., is directed by the physician to be used to make the solution isotonic, or in order to avoid an incompatibility between sodium chloride and other ingredients.) Divide the amount of sodium chloride in Step 4 by the sodium chloride equivalent of the substance used in place of sodium chloride. The quotient is the amount of that substance to be added to the prescription to make it isotonic.

SODIUM CHLORIDE EQUIVALENTS<sup>1</sup> FOR ISOTONIC COLLYRIA

	<i>NaCl</i> <i>equiv.</i>
Adrenalin (Epinephrine Hydrochloride)* . . . . .	0 26
Alum (Potassium) . . . . .	0 19
Alypin hydrochloride (Amydricaine Hydrochloride)* . . . . .	0 18
Ammonium chloride . . . . .	1 13
Amydricaine hydrochloride (Alypin Hydrochloride) . . . . .	0 18
Amylcaine hydrochloride (Stovaine)* . . . . .	0 20
Antipyrine . . . . .	0 17
Apothesine hydrochloride* . . . . .	0 19
Atropine sulfate . . . . .	0 14
Boric acid . . . . .	0 55
Butacaine sulfate (Butyn Sulfate)* . . . . .	0 10
Butamin (Tutocaine Hydrochloride)* . . . . .	0 20
Butyn sulfate (Butacaine Sulfate)* . . . . .	0 10
Chlorobutanol . . . . .	0 18
Cocaine hydrochloride . . . . .	0 19
Cupric sulfate . . . . .	0 15
Dextrose . . . . .	0 16
Dionin (Ethylmorphine Hydrochloride) . . . . .	0 16
Diethane hydrochloride* . . . . .	0 13
Ephedrine hydrochloride . . . . .	0 28
Ephedrine sulfate . . . . .	0 19
Epinephrine hydrochloride (Adrenalin)* . . . . .	0 26

	<i>NaCl</i> <i>equiv.</i>
Eserine salicylate (Physostigmine Salicylate) . . . . .	0.19
Eserine sulfate (Physostigmine Sulfate)* . . . . .	0.12
Ethylhydrocupreine hydrochloride (Optochin HCl)* . . . . .	0.15
Ethylmorphine hydrochloride (Dionin) . . . . .	0.16
Eucatropine hydrochloride (Euphtalmine)* . . . . .	0.18
Euphthalmine (Eucatropine Hydrochloride)* . . . . .	0.18
Fluorescein sodium* . . . . .	0.19
Glycerin . . . . .	0.35
Holocaine hydrochloride (Phenacaine Hydrochloride)* . . . . .	0.16
Homatropine hydrobromide . . . . .	0.19
Hyoscine hydrobromide (Scopolamine Hydrobromide)* . . . . .	0.13
Hyoscine hydrochloride (Scopolamine Hydrochloride)* . . . . .	0.15
Larocaine hydrochloride* . . . . .	0.18
Mercuric succinimide . . . . .	0.14
Metycaine hydrochloride* . . . . .	0.20
Mild protein silver (Argyrol) . . . . .	0.19
Morphine hydrochloride* . . . . .	0.15
Morphine sulfate . . . . .	0.15
Neosynephrin hydrochloride* . . . . .	0.22
Nupercaine hydrochloride* . . . . .	0.18
Optochin hydrochloride (Ethylhydrocupreine Hydrochloride)* . . . . .	0.15
Pantocaine hydrochloride (Tetracaine Hydrochloride)* . . . . .	0.19
Phenacaine hydrochloride (Holocaine Hydrochloride)* . . . . .	0.16
Pilocarpine hydrochloride . . . . .	0.22
Pilocarpine nitrate* . . . . .	0.21
Physostigmine salicylate (Eserine Salicylate) . . . . .	0.19
Physostigmine sulfate (Eserine Sulfate)* . . . . .	0.12
Potassium chloride . . . . .	0.84
Potassium nitrate . . . . .	0.60
Procaine hydrochloride . . . . .	0.24
Propadrine* . . . . .	0.31
Scopolamine hydrobromide (Hyoscine Hydrobromide)* . . . . .	0.13
Scopolamine hydrochloride (Hyoscine Hydrochloride)* . . . . .	0.15
Silver nitrate . . . . .	0.39
Silver protein, mild (Argyrol) . . . . .	0.19
Silver protein, strong (Protargol) . . . . .	0.04
Sodium bicarbonate . . . . .	0.69
Sodium biphosphate . . . . .	0.45
Sodium borate . . . . .	0.43
Sodium chloride . . . . .	1.00
Sodium nitrate (no H <sub>2</sub> O) . . . . .	0.62
Stovaine (Amylcaine Hydrochloride)* . . . . .	0.20
Strong silver protein (Protargol) . . . . .	0.04
Sucrose . . . . .	0.10
Syntropan* . . . . .	0.14
Tannic acid . . . . .	0.03
Tetracaine hydrochloride (Pantocaine Hydrochloride)* . . . . .	0.19
Tutocaine hydrochloride (Butamin)* . . . . .	0.20
Zinc chloride* . . . . .	0.60
Zinc sulfate . . . . .	0.15

## SODIUM CHLORIDE CONCENTRATIONS FOR ISOTONIC COLLYRIA

It has been determined by experiment that a solution containing 1.4 per cent of sodium chloride is isotonic with tears.

Therefore, 1 fluidounce of such a solution contains 6.37 or approximately 6.4 grains of sodium chloride.

30 cc. of such a solution contains 0.42 Gm. of sodium chloride.

### PRACTICAL EXAMPLES

R—Zinc sulfate	gr. i
Sol. of adrenalin (1 in 1000)	fʒ ss
Distilled water, q.s. ad	fʒ i
M. ft. collyr. isoton. cum sod. chlorid.	
Sig.—Drop in each eye as directed.	

*Step No. 1*

Zinc sulf. 1 gr. $\times$ 0.15	= 0.1500 gr. sod. chlor.
Adren. sol. (1/1000 $\times$ 30m) $\times$ 0.26	= 0.0078 gr. sod. chlor.

*Step No. 2* (add products in Step No. 1) = 0.1578 gr. sod. chlor.

*Step No. 3*—455 gr. (fl. oz.)  $\times$  0.014 = 6.37, or approx. 6.4 gr. sodium chloride needed alone to make solution isotonic.

*Step No. 4* (subtract Step No. 2 from Step No. 3).

6.4 gr. — 0.1578 gr. = 6.24 gr. sodium chloride are added to prescription to make it isotonic.

Same R to be made isotonic with boric acid instead of sodium chloride.

Steps 1-4 are the same as for sodium chloride.

*Step No. 5* (divide grains of sod. chloride in Step No. 4 by sodium chloride equivalent for boric acid. See table under Boric Acid.)

6.24 gr. NaCl  $\div$  0.55 = 11.35 gr. of boric acid added to prescription to make it isotonic.

Same prescription in the Metric System:

R—Zinc sulfate	0 06 Gm.
Sol. adrenalin, 1/1000	2 0 cc.
Dist. water, q.s. ad	30 0 cc.
M. ft. collyr. isoton. cum sod. chlorid.	
Sig.—Drop in each eye as directed.	

*Step No. 1.*

Zinc. sulf. 0.06 $\times$ 0.15	= 0 00900 Gm. sod. chlor.
Adren. sol. (1/1000 $\times$ 2) $\times$ 0.26	= 0 00052 Gm. sod. chlor.

*Step No. 2.*—(Add products in Step No. 1) = 0 00952 Gm. sod. chlor.

*Step No. 3.*—30  $\times$  0 014 = 0 42 Gm. sod. chlor. needed alone to make solution isotonic.

*Step No. 4.*—(Subtract Step No. 2 from Step No. 3).

0 42 — 0 00952 = 0 41048 or 0 41 Gm. of sodium chloride is added to the prescription to make it isotonic.

### REFERENCES

\* The above data without the asterisk are calculated from the freezing-point data by Husa and Rossi;<sup>2</sup> those with the asterisk are taken from Wells.

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NOTE.—This material has been abstracted from a report by R. Almin, published in Proceedings of the Minnesota State Pharmaceutical Association, p. 96 (1946).

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## COMMON LOGARITHMS

N	0	1	2	3	4	5	6	7	8	9
10	0000	0043	0086	0128	0170	0212	0253	0294	0334	0374
11	0414	0453	0492	0531	0569	0607	0645	0682	0719	0756
12	0792	0828	0864	0899	0934	0969	1004	1038	1072	1106
13	1139	1173	1206	1239	1271	1303	1335	1367	1399	1430
14	1461	1492	1523	1553	1584	1614	1644	1673	1703	1732
15	1761	1790	1818	1847	1875	1903	1931	1959	1987	2014
16	2041	2068	2095	2122	2148	2175	2201	2227	2253	2279
17	2304	2330	2355	2380	2405	2430	2455	2480	2504	2529
18	2553	2577	2601	2625	2648	2672	2695	2718	2742	2766
19	2788	2810	2833	2856	2878	2900	2923	2945	2967	2989
20	3010	3032	3054	3075	3096	3118	3139	3160	3181	3201
21	3222	3243	3263	3284	3304	3324	3345	3365	3385	3404
22	3424	3444	3464	3483	3502	3522	3541	3560	3579	3598
23	3617	3636	3655	3674	3692	3711	3729	3747	3766	3784
24	3802	3820	3838	3856	3874	3892	3909	3927	3945	3963
25	3979	3997	4014	4031	4048	4065	4082	4099	4116	4133
26	4150	4166	4183	4200	4216	4232	4249	4265	4281	4298
27	4314	4330	4346	4362	4378	4393	4409	4425	4440	4456
28	4472	4487	4502	4518	4533	4548	4564	4579	4594	4609
29	4624	4639	4654	4669	4683	4698	4713	4728	4742	4757
30	4771	4786	4800	4814	4829	4843	4857	4871	4886	4900
31	4914	4928	4942	4955	4969	4983	4997	5011	5024	5038
32	5051	5065	5079	5092	5105	5119	5132	5145	5159	5172
33	5185	5198	5211	5224	5237	5250	5263	5276	5289	5302
34	5315	5328	5340	5353	5366	5378	5391	5403	5416	5429
35	5441	5453	5465	5478	5490	5502	5514	5527	5539	5551
36	5563	5575	5587	5599	5611	5623	5635	5647	5658	5670
37	5682	5694	5705	5717	5729	5740	5752	5763	5775	5787
38	5798	5809	5821	5832	5843	5855	5866	5877	5888	5899
39	5911	5922	5933	5944	5955	5966	5977	5988	5999	6011
40	6021	6031	6042	6053	6064	6075	6085	6096	6107	6117
41	6128	6138	6149	6160	6170	6180	6191	6201	6212	6222
42	6232	6243	6253	6263	6274	6284	6294	6304	6314	6325
43	6335	6345	6355	6365	6375	6385	6396	6405	6415	6425
44	6435	6444	6454	6464	6474	6484	6493	6503	6513	6522
45	6532	6542	6551	6561	6571	6580	6590	6609	6618	6628
46	6628	6637	6646	6656	6665	6675	6684	6693	6702	6712
47	6721	6730	6739	6749	6763	6767	6776	6785	6794	6803
48	6812	6821	6830	6839	6848	6857	6866	6875	6884	6893
49	6902	6911	6920	6928	6937	6946	6955	6964	6973	6981
50	6990	6998	7007	7016	7024	7033	7042	7050	7059	7067
51	7076	7084	7093	7101	7110	7118	7126	7135	7143	7152
52	7160	7168	7177	7185	7193	7202	7210	7218	7226	7235
53	7242	7251	7259	7267	7275	7284	7292	7300	7308	7316
54	7324	7332	7340	7348	7356	7364	7373	7380	7388	7396
N	0	1	2	3	4	5	6	7	8	9





